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MASS X-RAY SURVEYS.¹

By H. W. WUNDERLY,
Canberra.

In this symposium on mass radiography I understand that you wish me to deal with the administrative aspects of mass surveys and to indicate what we are trying to do and what results are being obtained.

When miniature radiography was first introduced into Australia it was used for screening certain groups—namely, applicants for entry into the forces, and later all those engaged in the production of munitions. After the war this procedure, which had been used successfully in the screening of these groups, was extended to the general population and became known as "mass X-ray surveys". The Americans talk about "the community case-finding programme" and "the community-wide chest X-ray survey". At its last meeting the Standing Committee on X Rays of the National Health and Medical Research Council recommended that the term "case-finding programme for tuber-

culosis" would be more appropriate than "mass surveys", because this type of radiographic examination is being extended to certain groups such as in-patients of hospitals.

Before dealing with the purpose of mass X-ray surveys or the part they play in a case-finding programme, I want to make a short reference to the general plan for the control of tuberculosis. The objectives of this plan are: (i) prevention; (ii) to discover every person suffering from tuberculosis—that is, case-finding; (iii) to isolate and care for every person in need of medical treatment; (iv) to provide after-care and to rehabilitate every patient when this is possible; (v) to protect the patient and his or her dependants from economic distress.

This evening we are concerned with the role miniature radiography can play in assisting the case-finding part of this programme.

When applied to the general public, the primary object of the radiological part of case-finding surveys is to separate the "normals" from the "abnormals" amongst the apparently healthy, and I know of no other practicable method.

A case-finding survey can be planned to commence in one of two ways: (i) submit the whole population to a tuberculin skin test and limit radiography of the thorax to those giving positive reactions; or (ii) take a radiograph

¹ Part of a symposium on mass X-ray surveys, held by the Victorian Branch of the College of Radiologists of Australasia, September 22, 1953.

of the chests of all aged fourteen years and over, and confine the skin test in the first instance to children aged under fourteen years.

In countries like Australia, where the incidence of tuberculosis is relatively low, it would be satisfactory to perform a tuberculin skin test first and limit radiography to the positive reactors. This would bring to light the great majority of those who were suffering from tuberculosis or who had ever been infected with the tubercle bacillus. Administratively this would necessitate at least two visits of everyone to the centre—the first for the performance of the test and the second for its interpretation; the miniature radiographs could then be taken of the positive reactors, and B.C.G. vaccination could be offered to the non-reactors. However, as a nation-wide survey had never been made, it was decided to attempt to take an X-ray photograph of the chests of all members of the population aged over fourteen years. During these surveys many non-tuberculous conditions have been discovered, and if time permits I shall refer to some of them

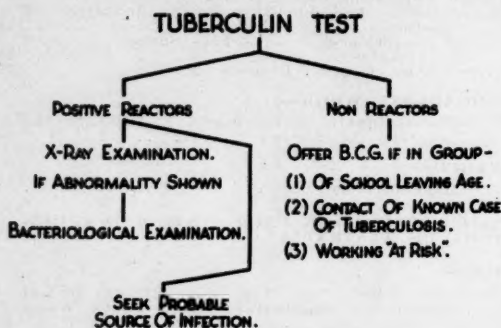


FIGURE 1.

later. It has been the experience here, as in most countries, that in many instances the disease has been detected when it is minimal in extent and in the earliest and most treatable stages. Also, especially in those areas where these surveys have been conducted on a compulsory basis, the very great majority of infective subjects have been detected. As the result of treatment and of education of these persons, the bacteria can be isolated from the remainder of the community and a definite step taken towards prevention.

Interpretation of Miniature Films.

The report on the miniature film should be expressed in the following terms: (i) "normal", which means no significant abnormality requiring further investigation; (ii) "probable abnormality"; (iii) "technical fault". It is recommended that large films should be taken of persons in categories (ii) and (iii). However, in some States the directors of tuberculosis are so satisfied with the technical quality of their miniature films that repeats of "technical faults" are taken again on miniature films, and they consider this practice quite satisfactory.

What abnormalities appearing in the miniature film can be regarded as of no significance and so not requiring further investigation?

It would be wrong even to appear to dictate to those interpreting miniature films; but it is my opinion that the following departures from normal can be regarded as insignificant and not requiring confirmation on a large film.⁽¹⁾

1. Lungs:

- (a) Anatomical abnormalities, such as azygos fissure or fissure of an inferior accessory lobe.
- (b) Small, localized emphysematous blebs or bullae without other abnormal findings.
- (c) Metallic foreign body with no other abnormal findings.

- (d) Slight or indefinite prominence of pulmonary markings consistent with variations in technique and age.

2. Pleura:

- (a) Apical pleural caps, without any indication of a parenchymal lesion.
- (b) Slight pleural thickening and adhesions, such as obliteration of the costo-phrenic sinus or thickening of the interlobar septum without the suggestion of possible effusion.

3. Mediastinal and Hilar Structures:

Single or multiple calcified foci.

4. Cardio-Vascular Structures:

Abnormalities in the contour of the heart or aorta; persons whose films show these should be referred for further investigation either by private practitioner or at a hospital.

5. Diaphragm:

- (a) Lobulations and serrations within normal limits.
- (b) Slight elevation. Those with eventration or possible herniation should be referred for further investigation.

6. Bony Thorax:

- (a) Congenital or developmental abnormalities of the ribs or other bony structures.
- (b) Fractures of ribs or clavicles.
- (c) Rib defects resulting from previous operations in the absence of pulmonary or pleural abnormalities.

7. Spine:

- (a) Congenital anomalies.
- (b) Arthritic changes.
- (c) Scoliosis.

8. Neck:

Calcifications in the lymph nodes, blood vessels or laryngeal cartilages.

Many will consider the presence of a few scattered calcified nodules of no significance, and others will require a lordotic view before saying "pleural caps" are of no significance. When I had the honour to address the members of this Branch of the College on a previous occasion I indicated how difficult, if not impossible, it was on radiological evidence alone to be sure that a particular opacity is caused by a lesion which is calcified and not merely caseous.

The very young and the very fat are unsuitable subjects for miniature radiography. It would not be tactful to exclude the latter from the "miniature" queue; but as quickly as possible they should be photographed on a large film as well.

It has been my experience that the deficiencies or mistakes connected with miniature radiography are more often due to errors in interpretation than to poor quality of films. In view of the rapid fatigue, retinal or other, which arises in the examination of large numbers of similar films, it is recommended that not more than 250 miniature radiographs per session of not more than one hour should be viewed by any one examiner, that no examiner should be engaged for more than two sessions of miniature film interpretation per day, and that at least two hours should elapse between sessions. "Because of personal errors which may arise in interpretation, it is recommended that each batch of miniature radiographs should be examined independently by at least two interpreters (one at least of whom should be a competent radiologist) skilled in the reading of chest radiographs and having had experience in the examination of miniature radiographs."⁽²⁾

In the past it was advised that "all cases regarded as suspicious by any one examiner should be investigated by direct radiography" on a large film. However, in some overseas countries it is the practice when any miniature film is regarded by both readers as requiring further examination on a large film for the large film to be taken. But when the two readers, on their first viewing, are not in agreement, they meet in consultation and if they are still unable to agree, the decision whether a large film will be taken or not is made by the director of the survey.

In some States it is customary for all subjects with normal findings on the miniature film to be notified accordingly. In all States any with probable abnormalities are requested to attend for the taking of a large film. It is at this attendance, marked "A" in Figure II, that an interview should be held with a trained nurse or medical social worker. A simple explanation of why a large film is necessary can be given and a few personal details noted. With six questions much information can be obtained and the answers can be entered on the card. In Figure III these questions are listed. They refer to a history of tuberculosis in the family, pleurisy, pulmonary tuberculosis, constitutional disturbances, cough and sputum.

Interpretation of Large Films.

The large film should be reported on in the following terms: (i) no significant abnormality requiring further investigation—usually reported as "normal"; (ii) abnormality confirmed with a description of its site, or indication of its site on the stamped thoracic outline, a short description of the appearances of the shadow, and mention

conducted on a compulsory basis the greatest care must be taken to maintain the private practitioner-patient relationship. Also those found to be suffering from non-tuberculous conditions must be referred to their private medical attendants or to hospital out-patient departments.

In Figures III and IV are shown the front and the back of a very suitable identification card to use in case-finding surveys. Not much information is required at the stage when the miniature radiograph is taken—the spool number, the frame number, the name of the subject and his address.

It is important to know when the last miniature radiograph was taken, and there is some necessity for having details about new arrivals in this country.

On the reverse side of this X-ray card (Figure IV) can be entered the report on the large film and the name and address of the usual medical attendant. For the sake of completeness the results of further investigations can be added, and if the final diagnosis is "tuberculosis" the details are then transferred to the Basic Index Card of the State Central Register.

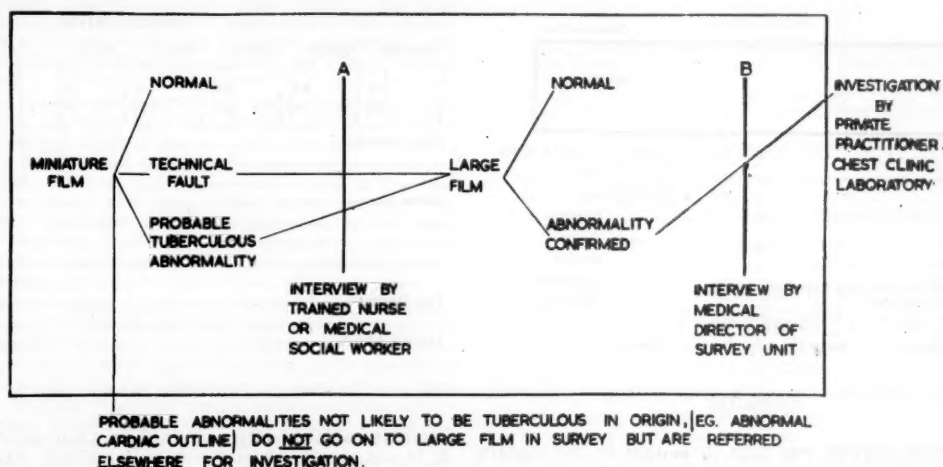


FIGURE II.

of the diagnostic probabilities with special mention of whether a diagnosis of tuberculosis is probable or not. All subjects whose abnormalities have been confirmed require further investigation of some sort or another. The presence of an abnormality having been confirmed on the large film, the subject should then be interviewed by the medical director of the survey unit, who will explain the necessity for and nature of further investigations. This interview is indicated by line "B" on Figure II. By giving these interviews at "A" and "B" much unnecessary anxiety can be avoided and greater cooperation obtained. The subject having been told of the necessity for further investigation, the part played by the mass X-ray survey unit in the case-finding programme ends. Naturally the unit will later be informed of the ultimate diagnosis and disposal of those with abnormalities confirmed on the large film. Everything within the rectangle of Figure II concerns the mass X-ray survey unit.

The ultimate success of these surveys depends on the completeness of the investigation of all "probably or possibly tuberculous" abnormalities. The subjects of these radiographs must be followed up till a definite diagnosis has been made. Whether in all instances the making of the diagnosis should be left to the Department of Public Health or some other authority responsible for the surveys is a matter for discussion. But in any case those found to be suffering from tuberculosis must be referred to their private medical attendants if they so desire, or to the nearest chest clinic, or to the out-patient department of an appropriate hospital or sanatorium. When surveys are

Group Surveys.

So far we have been considering the separation of those with normal chest radiographs from those with abnormal radiographs amongst the apparently healthy members of the community. After clinical and bacteriological investigation it is found that about one, two or three in every 1000 radiographically examined are suffering from tuberculosis in a form which needs treatment.

There are certain groups in which it is known that the incidence of tuberculosis is likely to be higher.

It has been found that amongst patients referred by private practitioners the incidence of tuberculosis is about ten times that detected amongst the apparently healthy members of the community. The radiological examination of the lungs of all in-patients and of all patients newly admitted to hospital, as well as bringing to light many unsuspected cases of tuberculosis, is designed to protect members of hospital staffs and other in-patients from exposure to undetected disease, and is established hospital policy in many parts of the world. In 1947, Dr. J. Lindell, when medical superintendent of the Royal Melbourne Hospital, wrote an excellent article on the importance of this investigation. Once this examination of all in-patients has been put into operation, a similar examination of all out-patients should be undertaken. It is a good plan to begin with all out-patients who have been attending for five years or more and all who are attending for the first time. The results of these examinations provide many surprises. These two groups—(i) patients referred by

private practitioners and (ii) in-patients and out-patients of hospitals—consist of people we can class as “apparently ill” as opposed to the previous class of “apparently well”. Other groups which should be investigated are the following: (iii) all contacts, domiciliary and other, of all known subjects of tuberculosis; (iv) all women attending pre-natal clinics; (v) applicants for employment in the various public services, in industries *et cetera*, and national service trainees; food handlers; (vi) all hospital employees and applicants for such employment, the mental hospitals included; (vii) all whose duties bring them into close contact with children; (viii) miners and employees in industries where there is a dust hazard.

The following figures relate to mass surveys conducted in Australia: (i) in country areas, of approximately 50,000 examined, 0.03% had proven pulmonary tuberculosis; (ii) in city areas, of approximately 74,000 examined, 0.1% had proven pulmonary tuberculosis; (iii) in congested suburbs, of approximately 101,000 examined, 1.43% had proven pulmonary tuberculosis; of 154 proven cases, 143 were previously unknown to the authorities.⁽⁵⁾ The “yield” in

is cavitation with or without fluid level, pleural effusion or a pneumonic process. “If a survey succeeds in detecting those in need of immediate medical care and those who need further investigation and follow-up, it may be said to have achieved its objectives.”⁽⁶⁾

It is frequently stated that there is no sense in going on with these case-finding programmes, because already there are not sufficient beds to accommodate the known tuberculosis subjects. Surely there is no substance in this argument. It is not necessary to put every person suffering from tuberculosis into a sanatorium; some can be safely put to bed at home while waiting for a sanatorium bed to become available. By education alone much can be done to isolate the bacilli.

How frequently community-wide case-finding surveys should be repeated I do not know. Some think the ideal would be to make them annually. It has been the experience in some areas where surveys have been repeated after twelve months that very many fewer new cases were detected than during the first survey. It has been found that once an industry has been surveyed and all new

Date _____ District—Town _____

Surname _____ Age _____ years Last M.R. Exam. _____
First Name _____ Sex ☐ M ☐ F Date _____
Second Name _____ M ☐ S ☐ W No. _____
Occupation _____ Disposal—_____
Postal Address _____ Doctor _____
M.R. Report _____ Hospital _____
Country of Birth _____ Sanatorium _____
Date of Arrival in Australia _____ Chest Clinic _____
FH ☐ PI ☐ FTb ☐ C ☐ Cough ☐ Sputum ☐
Normal ☐ Abnormal ☐ Repeat ☐ Large Film ☐ Incomplete ☐ No Action ☐

FIGURE III.

the congested suburbs was fifty times that in the country areas.

It may interest members of this Branch of the College to learn that in the United States of America the Federal Security Service, under which the Division of Tuberculosis and Chronic Diseases operates, has, in order to conserve its finances, decided to discontinue its assistance to the States for community-wide surveys. This also has happened in various parts of Great Britain and may happen here, though support would be continued for the radiological and other examination of the eight groups just mentioned.

In Great Britain, Canada and the United States of America private practitioners are making increasing use of the chest X-ray service offered by public health authorities. Some refer only those patients whose symptoms suggest that they may be suffering from some disease of their respiratory organs. Others advise all their private patients to have at least one X-ray photograph of their lungs taken every year.

As the result of these investigations it has been noted that many more who complained of digestive disturbance were found to be suffering from active tuberculosis than were those who complained of cough. I have always said that patients who have pleurisy or who cough up blood are lucky because their lungs are almost certain to be radiographically examined; but many who complain of lassitude or indigestion or both are not so fortunate. However, during X-ray examination with a barium meal, most radiologists now examine the lungs fluoroscopically to make sure that disease above the diaphragm is not the cause of symptoms below.

After inspection of the large film it is often possible for the “reader” to indicate that the subject of the film is in urgent need of investigation—for example, when there

INVESTIGATION

Tuberculin	Sputum	Gastric	B.S.R.	B.C.G.
1	1	1	1	1
2	2	2	2	2
3	3	3	3	3

X-Ray Report—_____

Clinical Notes—_____

Final Diagnosis—_____

Doctor's Address—_____




FIGURE IV.

entrants radiologically examined on their admission to it, it is not worth while again radiologically examining all employees in that industry.

When discussing the interpretation of miniature radiographs I mentioned the numbers which could be read in one hour—namely, 250. This referred to the interpretation of films connected with mass surveys of the general population. When one is viewing films of persons who are apparently ill, such as hospital patients and patients referred by their medical attendants, it is thought that not more than 200 miniature radiographs should be interpreted in an hour. Of large films, 25 could be reported on in an hour, but only 15 if the subjects were in the “apparently ill” groups. I feel it is not a good plan to continue in this way—it is wise to limit the number of miniature films which should be reported on in a session of one hour; but when it comes to large films, I think it would be wise to fix a fee for each hour's reporting and not attempt to assess the number which should be reported on in an hour. So much depends on the number of “abnormals”.

Nor do I think it right that “readers” should express the opinion that a miniature or a large film should be “repeated” after an interval of three, six, nine or more months. If there is a “probable abnormality” in the miniature film, a large film should be ordered. It is not for the radiologist or chest physician reading a large film in connexion with a survey to decide the necessity for a further film after a stated interval. That decision must be made by the one who has the results of all the investigations available to him.

What Mass X-Ray Surveys are Achieving.

Mass X-ray surveys initiate the investigation which leads to the detection of many previously unknown cases of

tuberculosis amongst the apparently healthy and amongst members of the groups mentioned earlier this evening. Also many non-tuberculous conditions are discovered.

Except in the remote country areas, the number of persons found after investigation to be tuberculous and in need of treatment varies from one to three of every 1000 radiographically examined; about five or ten times this number require supervision.

I do not wish to stress the matter of cost, because every unknown infectious case which is brought to light can be converted into one less source of infection in the community—so finding it is worth while. But it should be realized that some infectious cases are costing over £1000 to locate, whereas others cost less than £50. Not only are these comparatively isolated cases expensive from the point of view of pounds, shillings and pence, but their detection keeps the equipment and trained staff away from more productive fields for long periods.

If you asked me where I think our attack should be concentrated I would suggest the groups already mentioned and limit community-wide surveys to our cities and overcrowded, poorly housed suburbs. Only when these have been completely surveyed would I start on our more remote areas, where in any case the hospital population and patients of private practitioners should be under regular surveillance.

A survey works most efficiently when processing and interpretation are done at a central office or depot. Much of the educational value of the survey is lost if the readers of the large films do not have the corresponding miniature films available to them for comparison. This is the best way to learn about over-reading and under-reading. In addition, the "readers" should be informed of the final diagnosis. In this way what may appear a very dull routine can be turned into a measure of great educational value to us all.

In countries where there are well-staffed and well-equipped chest clinics outside the capital cities, most of the investigation onwards from the miniature film stage is carried out there. As a large proportion of the miniature film readers at the central depot are full-time officers, they spend some of their time visiting the outside clinics, follow up the further investigations *et cetera*, and so conduct a widespread educational service. The possibility of instituting such a service in this country is worthy of our deepest consideration.

Conclusion.

In conclusion I should like to say a few words about the non-tuberculous conditions found during mass surveys. The two most important groups are cardio-vascular diseases and cancer. I do not know of any mass surveys which have been conducted specifically to locate sufferers from these conditions; but during surveys originally instituted for tuberculosis case-finding, special efforts have been made to detect these other conditions. On July 4, 1953, there appeared in this journal a paper in which two such surveys were analysed (Proust⁽⁴⁾). In one survey, out of 500,000 miniature films, only 22 persons found to have cancer of the lung were considered to be operable. In the other, 85% of those who were thought to have abnormal cardiac or aortic silhouettes in the micro film were later proved to have organic heart disease. It has been said that abnormal contour is of more importance than abnormal size of the heart.

Summary.

All that I have said this evening can be summarized as follows:

1. The function of the radiological part of case-finding programmes is to separate the normals from the abnormal.
2. Mass miniature radiography is the only practicable way of detecting probable tuberculosis amongst the apparently healthy members of the community.
3. All significant probable abnormalities in the miniature films should be further examined on large films.

4. All subjects whose probable abnormality is confirmed on a large film should be referred for further investigation; once that recommendation has been made, the radiological part of the mass survey ends.

5. This investigation should include thorough clinical and bacteriological examination, and it is the responsibility of the chest physician to recommend the patient's disposal and future observation.

We must remember that radiography is only a part, though a very important one, of a case-finding programme, and that miniature radiographs, if of poor technical quality or if poorly interpreted, are dangerous, but if of good quality and if correctly interpreted, can make a tremendous contribution towards the control of tuberculosis in our midst provided they lead to thorough investigation, clinical and bacteriological.

Acknowledgement.

I wish to acknowledge the permission of Dr. A. J. Metcalfe, Director-General of Health, to submit this article for publication.

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TECHNICAL ASPECTS OF MINIATURE RADIOGRAPHY.¹

By C. E. EDDY,

Director, Commonwealth X-Ray and Radium Laboratory, Melbourne.

THE use of the miniature film in case-finding programmes for tuberculosis involves the photography on fine-grained film, with cameras of wide aperture, of the image of the chest produced on the fluorescent screen. Originally, commercially available screens, cameras and film were used in association with ordinary diagnostic X-ray equipment. Successive developments have taken place to produce X-ray equipment specially designed for routine chest radiography, together with fluorescent screens particularly efficient in the actinic region, films sensitive in this region, and camera lenses designed for short-distance operation. As a result the technical standard of the miniature radiographs obtained has improved very considerably.

The modern X-ray unit for case-finding consists essentially of the following: (i) a four-valve transformer unit delivering at least 200 milliamperes at 100 kilovolts; (ii) a simplified control stand giving about three ranges each of tube voltage and current, and providing for photo-electric timing of exposure; (iii) a rotating anode tube (preferably with blower) and a camera tunnel readily positioned in correct alignment, and arranged (either by means of a moving platform for the patient or by moving columns carrying the tube and tunnel) to require only one adjustment of height to suit each patient; (iv) a camera, fitted with at least an f/1.5 lens or mirror system, and using a length of film, the film preferably moving on automatically after each exposure; (v) a card illumination system, whereby the patient's name and serial number are photographed on the radiograph, thus making identification simple and certain; (vi) systems of automatic relays, which require that a fresh area of film is in position and a new

¹Part of a symposium on mass X-ray surveys, held by the Victorian Branch of the College of Radiologists of Australasia, September 22, 1953.

patient's card has been inserted before an exposure can be made.

The unit may be made up of components designed for ready dismantling and reassembly in halls *et cetera*. Only a very small number of the units in use by any one authority need be permanently mounted in caravans or trucks.

The development of X-ray equipment for case-finding has had some unique features, and these have led to some interesting trade reactions. Initially, d'Abreu announced his method of mass survey using normal commercially available components, and from his experience suggested the desirable details of special equipment. In most countries the purchasers of this equipment were not private individuals, but government bodies who invariably obtained expert advice in formulating "user" specifications for the equipment required. The manufacturers were then probably for the first time presented with orders for equipment for which they had made no sales efforts. It was probably inevitable that some manufacturers should then endeavour to make variations in these specifications for which they could then claim certain advantages over the products of their competitors. Most of these variations took place in the camera system employed, and possibly the variations, and some of the entirely unscientific claims made for them, have led to much of the present confusion which exists regarding the most suitable size and type of film. It therefore seems desirable to discuss in some detail the requirements of the camera system, and the methods of satisfying these.

It must, in my opinion, be accepted that the purpose of the miniature film is to select cases for further investigation (by radiography on full-sized film, clinical and bacteriological examinations *et cetera*). Probably 98 out of every 100 miniature films are reported as "normal" and are then of no further use. Any arguments regarding the size of the miniature film in a case-finding programme, based on the convenience of the film for filing with the patient's records, are therefore irrelevant.

The necessary conditions for the camera unit are therefore as follows: (i) a large aperture optical system suitably corrected for the short object-film distance used; (ii) an efficient fluorescent screen with as fine a grain as possible; (iii) a fast but fine-grained photographic emulsion; (iv) a roll-type film with proper safeguards for ensuring that the film is accurately positioned in the focal plane during exposure.

It is frequently not realized that all types of camera lenses of the same aperture do not necessarily give the same performance. The primary lens must be suitably corrected for a number of aberrations, and the difficulties in making these corrections increase with the aperture of the lens. The corrections to be made depend to some extent on the object-film distance used, so that lenses designed for long-distance photography are not always suitably corrected for the usual miniature camera tunnel distance of less than three feet. For this reason it was not unexpected that high aperture lenses designed for aerial photography did not give a good performance at a close distance.

The excellence of the optical and photographic system can be tested by physical means. It has been shown definitely that the resolution obtained (in lines per millimetre on the fluorescent screen) with 35-millimetre film, when a variety of good lenses of a focal length of five centimetres available commercially are used, is superior to that obtained with either the 70-millimetre Fairchild camera or the 100-millimetre G.E. camera. These larger films therefore do not show more detail. They may be viewed more conveniently, but the detail is distinctly inferior.

The prime purpose of the miniature film is to select abnormal subjects requiring further investigation. Because of statements that miniature films of a larger size were more reliable in selecting abnormal subjects, two carefully planned investigations were made in the United States in which many hundreds of patients were radiographed in turn on miniature film of different sizes, and on full-size

paper and film. All these films were then reported upon at intervals by a panel of experienced radiologists and chest physicians, and an analysis was made of the selection of abnormalities from each size of film. In both investigations it was concluded that for the purpose of selecting subjects for investigation no one size of film was more accurate than any other.

It is generally agreed that no attempt should be made to form a diagnosis upon anything less than a full-size radiograph.

It was for these scientific reasons that the Standing Committee on X Rays of the National Health and Medical Research Council recommended some years ago that for case-finding programmes the 35-millimetre film was to be preferred, being equally accurate, considerably cheaper and more convenient.

Within the last few years optical systems in which mirrors have been used instead of lenses have been developed for miniature radiography. These can now be regarded as having passed the experimental stage. The Commonwealth X-ray and Radium Laboratory has had experience with cameras of this type in actual surveys and is satisfied with their performance.

The mirror camera has certain definite advantages over the lens camera. The image detail is as sharp as, if not sharper than, that obtained with even the best lens. The illumination over the whole field is much more uniform. But—and this is the most important point—it is possible for approximately the same expenditure to obtain a mirror camera with a speed of from six to eight times that of a lens camera. This increased speed enables an X-ray plant of much smaller capacity (and therefore smaller size and cost) to be used, and this is a great advantage in locations in which the electric supplies are not adequate for higher-powered units.

Mirror cameras of slightly different design have been developed by at least three manufacturers. These manufacturers have not adopted a standard of one size of film, but can supply cameras for either 35-millimetre or 70-millimetre film, and in one case for 45-millimetre film.

It has become obvious that the size of the film (that is, its width) is not a satisfactory method of indicating the size of the chest image obtained. In my opinion one should specify not the size of the film, but rather the size on the film of the image of, say, a 16 inch by 16 inch fluorescent screen. There has been an appreciable variation in the size of the image as given by the equipments of various types, as will be evident from the figures in Table I.

TABLE I.

Size of Film.	Size of Image.
1. 35 mm. perforated	24 by 24 mm.
2. 35 mm. unperforated	30 by 30 mm.
3. 45 mm. unperforated	38 by 38 mm.
4. 70 mm. perforated	54 by 54 mm.

It should be noted that by the use of cameras in which unperforated instead of perforated 35-millimetre film is employed, the image can be increased by 25%.

It should also always be stated what optical system is being used. Physical tests of detail show that films from the Schonander or Odelca 70-millimetre mirror cameras are superior to those from the Fairchild 70-millimetre lens camera, while the five inch by four inch film from the Watson London lens camera is very much superior to that from the Watson Victor camera of the same size.

Whatever X-ray unit or camera system is employed, the miniature radiographs obtained are still largely the result of care and skill on the part of the radiographer and the dark-room attendant. The positioning of the patient must be carried out in miniature radiography possibly even more carefully than in direct radiography, because the increased magnification at shorter distances may mean that the apices or bases of the lungs fall outside the

fluorescent screen. Visibility of identification of the card number depends upon the sharpness and blackness of the figures placed on the card. Jamming of film (and damage to the film transmission system) can arise through careless and clumsy loading of the cassettes. The use of too low a tube voltage leads to longer exposures with possible movement of the patient and risk of overheating of the tube. Although the use of the photo-electric timer and the various automatic devices has reduced the need for the radiographer to think about certain factors, there are still many and important factors which require his careful attention. There are some of us who feel that there is a danger that too many foolproof devices may even lead to the development of fools.

It is still true that many films are spoilt in the dark-room. Miniature films, frequently being panchromatic and therefore able to be developed only in complete darkness, cannot be developed by inspection. Standardized conditions of time, temperature and age of developer must be rigidly followed, while the greatest care must be taken in washing, drying and preparing films for reporting.

The maintenance of a high technical standard in the films being produced is an ever-recurrent problem in radiography. This is a much more difficult matter in chest surveys than in hospitals or private practices. In the hospital all films are viewed by an experienced radiologist in circumstances which enable a faulty film to be associated with a particular radiographer. Senior and experienced radiographers are available to assist in overcoming the fault. In general, in mass surveys, this association of the faulty film with a particular radiographer is more difficult, and special precautions should be taken to overcome this difficulty. It should be accepted that, with the provision of so many automatic devices, the maintenance of a high technical standard in a mass survey should be easier than in a hospital.

I have for a long time been concerned at the way in which the technical standards in mass radiography can deteriorate to an appreciable extent without this deterioration being observed. I have discussed this point with well-known authorities overseas, and they agree with me as to the general principles which must be followed to prevent this deterioration. It seems impossible to rely on the individual readers of films to do more than report "technical faults". Too often the reader is inclined to presuppose some excuse for technical faults (sudden rush of patients *et cetera*), or through naturally concentrating on his own problem of reading the films to fail to notice that the proportion of technical faults is steadily increasing.

In the first instance, definite radiographic and dark-room procedures should be laid down, and the senior radiographer with each unit should be responsible for full observance of these. Secondly, typical samples of films from every unit operating in the survey should be examined, preferably by an experienced radiologist, solely to observe technical standards. His experience should enable him not only to detect a technical fault, but to suggest the cause and the means of eliminating it. He will also know from experience that the overlooking of some faults in positioning this week will lead to an increasing number of such faults next week. If necessary, the number of faults in the work of a team should be regarded as a reflection on the team itself—the natural *esprit de corps* within the team should be encouraged and a healthy rivalry as to technical work would be no disadvantage.

In insisting on a rigorous observance of operating procedures as laid down, I am in no way wishing to limit any useful suggestion for any improvement in technique. However, it is essential that any suggested alteration in technique should be approved, and satisfactory control conditions set up to test the improvement. Mass surveys as they are operated throughout the world give greater freedom from immediate supervision to individual radiographers than occurs in hospitals, but this should be accompanied by a greater sense of responsibility. In hospitals (and in private practices) every film (often in a wet condition) is seen by a radiologist and no changes in technique are made without discussion and approval. I

am sure that in many cases changes of technique have occurred in mass surveys without such approval, and often on quite incorrect grounds. Camera settings have been altered to improve focusing when no satisfactory means have been available of showing that the existing focusing was faulty, or that the new focusing was an improvement. Changes have been made in the type of film used without any scientific tests as to its suitability. Changes have been made in exposure and developing technique. In many cases these changes have been made without a full appreciation of their physical effect. In some cases technical faults (particularly in positioning) have resulted from attempts (sometimes by lay supervisors) to "speed up" the flow of patients undesirably. In others, a poor technical standard has resulted from alterations in the time and type of development, with a resultant deterioration in photographic quality. The use of old developer, possibly urged on grounds of economy, can more readily result in "flat" radiographs with panchromatic than with ordinary X-ray film. Frequently voltages are reduced without its being realized that the fluorescent screen can tolerate higher voltages for correct quality than does the photographic film. The inability of the photo-electric timer to compensate for the natural period of the main contactors with thin patients is often overlooked, or is compensated for by a reduction in tube voltage rather than by a reduction in tube current. In some cases the increased speed of cameras of the mirror type has not been appreciated, and efforts then made to use very high tube currents have resulted in over-exposed radiographs.

Individual radiographers are rarely permitted to make sweeping changes in technique in hospitals without full discussion and approval. They should not do so to any greater extent in a mass survey scheme.

In England, much has been done to maintain the technical standards of units operating under various local authorities at a high level. Each operating team is first trained at a central depot until the desired standard of competency has been achieved. Thereafter sample films are returned regularly from each unit to the depot, where faults are noticed and methods of remedying them formulated. Persistently poor standards result in the withdrawal of the team for further training. The high standard achieved in the miniature films taken in Sweden and Denmark is also due to a similar rigorous checking of the work of every team.

It must be admitted that the rapid development of mass schemes for chest surveys led to the need for the development of special equipment and of specially trained radiographers. The financial incentive has led manufacturers to produce suitable equipment. It is possibly in the supply of trained radiographers and in the improvement of technical standards in the films produced that further developments should be expected in the future.

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I wish to thank the Director-General of Health, Dr. A. J. Metcalfe, for permission to submit this paper for publication.

CHEMOTHERAPY IN TUBERCULOSIS.

By HILARY ROCHE,

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A RECENT visit to the United Kingdom, Ontario (Canada) and the United States of America shows that the chemotherapy of tuberculosis in these countries follows on the whole the same general lines.

In the United Kingdom there is still a tendency to give streptomycin (sulphate) daily, rather than on the bi-weekly basis, which has been the practice for the past three years in North America.

The use of preparations consisting of half streptomycin sulphate and half dihydrostreptomycin sulphate is coming more and more into favour, especially in conditions where prolonged daily therapy is indicated. It is held that this combination reduces the incidence of vestibular and auditory disturbances without loss of therapeutic effect. Further, dihydrostreptomycin is often given to patients who show signs of intolerance to streptomycin.

Prolonged chemotherapy is now generally accepted as essential, the minimum period being four months, administration for from nine to twelve months being quite common, with sometimes prolongation to eighteen months and two years.

At present trials are being carried on by the Veterans' Administration in the United States of America to obtain some guidance as to the desirable duration of treatment in different types of cases. One group of patients is continuing to receive treatment for three months after the target point has been reached, a second group for six months, and the third group for nine months after. The "target point" has been defined as the stage when the following conditions exist: (i) negative response to bacteriological tests for three months; (ii) no demonstrable cavitation; (iii) stabilization of radiological shadows. A preliminary report on these trials is expected early in 1954.

It is everywhere common practice to prescribe streptomycin daily in such serious conditions as miliary and meningeal tuberculosis and during the most acute phase of other tuberculous manifestations. Almost invariably PAS (12 to 18 grammes of the sodium salt) is given daily by mouth in order to retard the development of bacterial resistance to streptomycin. INH (usual dose three to eight milligrammes per kilogram of body weight) is used in some centres with streptomycin and PAS (a) as a routine in every case, or (b) in others only in the most serious forms of the disease. INH may be held in reserve for emergencies or employed to replace PAS when this is poorly tolerated.

It would seem desirable, in the present state of our knowledge, to use INH only in the most serious forms of the disease, or when PAS cannot be taken, and never alone. At times, however, especially in the treatment of patients at home, it may not be convenient to give injections of streptomycin even twice weekly. In such cases INH can be combined with PAS.

If streptomycin is given daily during the initial period of treatment, bi-weekly administration is begun as soon as the more acute phase of the disease has passed. The usual adult dosage is one gramme. Clinical and experimental evidence shows that bacterial sensitivity to these chemotherapeutic agents tends to persist for longer and in a higher proportion of cases when at least two of these agents are prescribed together.

It should be noted that the clinical significance of in-vitro sensitivity tests is by no means fully understood. Both sensitive and insensitive bacilli have been found in the same specimen of sputum and in the same focus of disease in resected specimens. Further, even if insensitive bacilli are being discharged in the sputum, sensitive bacilli can coexist in other foci in the lungs which do not open into a bronchus, and in other parts of the body. Occasionally anatomical factors, especially inadequate circulation, will prevent a completely successful response, even if the bacilli are sensitive. Bacilli insensitive to one drug may be susceptible to the synergistic activity of two or more. In the case of persistent cavitation, bacilli tend to become more rapidly insensitive. Sometimes, though the disease may still be active, it may become impossible after some weeks of chemotherapy to cultivate any bacilli. In other instances bacilli may be found on examination of smears, but chemotherapy has so altered their cultural requirements that they grow with difficulty, if at all.

Successive laboratory tests may also show fluctuation in the degree of sensitivity. However, in the recent Medical Research Council trials reported in *The Lancet* of August 1, 1953, bacilli which had become insensitive to INH were no less so three months after treatment had stopped.

Many clinicians believe that patients discharging bacilli insensitive to 100 microgrammes of streptomycin per millilitre do not as a rule respond to further therapy with streptomycin—for example, during relapses following surgical intervention—and for this reason any operation should be performed while the bacilli are still sensitive to streptomycin. On the other hand, there is evidence to suggest that pronounced loss of sensitivity to INH may in some cases be associated with some loss of pathogenicity. There is still much conflict of opinion about this, and much more animal experimentation and many more clinical observations are required. In any case, so long as the patient appears to be responding, the treatment should be continued even if in-vitro tests indicate that the bacilli have become insensitive.

With regard to chemotherapy in relation to surgical intervention, thoracic or otherwise, it is important that operation should be carried out while the bacilli are still sensitive, at least to streptomycin. At the beginning a tentative plan with reference to the operation should be drawn up. Specific medication, combined with a general sanatorium régime, is prescribed to prepare the patient for surgery. This preparatory stage may last for from three to six months or longer. The time for intervention has obviously to be decided by individual considerations. A balance has to be struck between the maximum benefit obtainable by such preliminary chemotherapy and the risk of emergence of insensitive strains of bacilli. The chemotherapy is continued after operation for varying periods according to individual indications. Specific antibacterial treatment has been found to lessen the need for surgery in bone and joint tuberculosis. On the other hand, it has made possible the more frequent excision of pulmonary lesions.

Indications for Chemotherapy.

For children aged five years and under, antibacterial therapy should always be prescribed, whatever the manifestation of the disease. From older children, in the presence of relatively insignificant disease running a favourable course, chemotherapy is sometimes withheld. The majority of clinicians, however, are inclined to treat with specific medication all active tuberculous manifestations, even if they are of no apparent serious significance. This practice includes patients of all ages. It would certainly seem prudent to treat with chemotherapy any recent tuberculous lesion, even if minimal in extent and not obviously cavitated.

As was mentioned earlier, daily administration of streptomycin is reserved only for the most serious cases, and a change to bi-weekly administration should be made as soon as possible. This method can generally be adopted without loss of therapeutic effect, with diminished risk of complications, and with greatly reduced chances of bacilli losing sensitivity.

Tuberculous Meningitis.

In the centres visited, streptomycin and INH are given as a routine, usually with PAS, except at Oxford and the National Jewish Hospital, Denver. Dosage varies with age and body weight. Everywhere streptomycin is given daily in two or three divided doses by the intramuscular route, and in some centres, notably Oxford, intrathecally as well. At Oxford also Dr. Honor Smith advises the intrathecal (and sometimes intraventricular), as well as oral, administration of INH, and the intrathecal injection of tuberculin in the form of P.P.D. While streptomycin and INH are given daily, P.P.D. is prescribed intermittently, the dose and frequency of administration being decided by the sensitivity to tuberculin and the reaction in the cerebro-spinal fluid, as determined by daily counts of the cells and estimations of the protein.

Most clinicians believe that this treatment, exacting for both the patient and staff, is as a rule not indicated in tuberculous meningitis, except possibly in the presence of block to the circulation of the cerebro-spinal fluid. As INH has the power of intracellular penetration, it is generally held that the addition of this powerful agent to

streptomycin represents the maximum in present-day therapeutic efficiency. However, it should be recognized that Dr. Honor Smith, with her multiphasic offensive tactics, has had some remarkable results in cases generally recognized as hopeless. She also is most insistent that success in the treatment of tuberculous meningitis depends essentially on early diagnosis. It is agreed everywhere that treatment must be prolonged, the minimum period being twelve months. The duration of intrathecal therapy depends on the result of frequent examinations of the cerebro-spinal fluid, in particular the total protein content and the cell count.

Some Other Tuberculous Manifestations.

In the treatment of pleural effusion the Veterans' Administration is at present advising the bi-weekly administration of streptomycin with 12 grammes of PAS daily for a period of from four to twelve months. In the case of genito-urinary tuberculosis, the administration of streptomycin bi-weekly and PAS daily is the commonest form of chemotherapy; but the Veterans' Administration is trying the combination of streptomycin given bi-weekly with INH given daily (300 milligrammes) for at least twelve months.

Unconventional Chemotherapy.

1. At the National Jewish Hospital, Denver, Colorado, the practice of chemotherapy is based on Dr. Gordon Middlebrook's animal experimentation and clinical research. It consists essentially of the following: (i) the use of streptomycin without PAS for a short period (three to four weeks) at the beginning of treatment; (ii) administration of INH (four milligrammes per kilogram of body weight for the first two or three days), beginning on the third day; (iii) the long-continued employment of INH (one to two years) in relatively high dosage—eight milligrammes per kilogram of body weight without any other antibiotic, except streptomycin as above. Dr. Middlebrook believes that bacilli insensitive to INH in strengths of 10 microgrammes per millilitre or higher do not cause visceral disease in experimental animals, when infection is airborne or induced by subcutaneous inoculation. Spread of disease in patients carrying very insensitive strains has not been observed at this hospital, and such bacilli are probably non-pathogenic to man. In INH therapy, according to Middlebrook, it is desirable, therefore, to induce a high degree of insensitivity as soon as possible, and this apparently can be brought about by high dosage. Bacilli insensitive to one microgramme per millilitre still retain some pathogenicity.

Control over the disease has, according to the views held at this hospital, been so improved by the use of streptomycin and INH that the great majority of patients can safely be allowed greater physical activity much earlier, without risk of relapse or of delaying retrogression of the morbid process. A very active rehabilitation and social programme is a special feature of the hospital.

Surgical extirpation of all significant residual lesions is practised when possible after the maximum benefit appears to have been obtained by chemotherapy.

2. At Olive View Sanatorium, Los Angeles County, the unorthodox attitude to chemotherapy has been influenced by the experimental work of Dr. Emil Bogen, Director of Research, and by clinical observation. At Olive View it is the usual practice to give the specific medication only twice weekly and eventually only on one day per week—all three agents (streptomycin, PAS and INH) on the same day. At the onset, in acute or severe disease, such as military tuberculosis or tuberculous meningitis, they are given daily.

3. The results obtained in tuberculous meningitis by the combination of tuberculin and specific medication have prompted a trial in Oxford of the same combination in other forms of the disease, such as pulmonary and inoperable genito-urinary tuberculosis. A few promising results have been noted, but there is as yet no valid evidence to suggest that this line of treatment should be more generally

adopted. Resolution of fibrinous exudate due to the action of tuberculin can readily be imagined, whereas such a process in the case of organized fibrotic tissue would appear impossible. However, some resolving action may still be possible before organization is very far advanced.

4. Cortisone and ACTH are being used in a few centres in conjunction with antibiotics, not only in the treatment of obvious intolerance to streptomycin, but also to limit the inflammatory reaction in some conditions such as pericarditis, meningitis *et cetera*. There is ample experimental and clinical evidence of the grave danger of employing cortisone or ACTH alone in the presence of latent or active tuberculosis. However, under cover of specific chemotherapy there seems to be a very limited and presumably safe field of usefulness for them, provided that the dosage is small, clinical supervision is very close, and the period of administration is curtailed. These powerful, potentially dangerous substances must be used with the greatest caution, and it would appear safer for us to wait until more widespread trials have been made.

Toxic Effects.

The larger the dosage and more frequent the administration of streptomycin, the greater the possibility of toxic effects, particularly on the eighth nerve—the vestibular branch in the case of ordinary streptomycin, the auditory branch in the case of dihydrostreptomycin. (It is customary in some hospitals to examine vestibular function and conduct audiometric tests once every three months on patients receiving streptomycin or dihydrostreptomycin.) Otherwise, the most common complications of streptomycin therapy appear to be due to hypersensitivity to the drug, paræsthesiæ (numbness and tingling), albuminuria, rashes, fever *et cetera*.

With PAS a wide variety of toxic manifestations have been reported—fever, skin eruptions, anaemia, agranulocytosis, jaundice, diminution of blood potassium content, psychosis *et cetera*. However, these occur relatively infrequently, and their appearance should be an immediate indication to stop administration of PAS. Gastro-intestinal irritation with anorexia and a tendency to diarrhoea are not uncommon and may necessitate a cessation of treatment for one or two days occasionally. The concomitant use of "Benemid" has been advised in the treatment of patients who are particularly intolerant from the gastro-intestinal point of view.

It seems that when "Benemid" (2.0 to 2.5 grammes for an adult) is given, it is possible to halve the dose of PAS and yet obtain serum levels comparable with those obtained on full doses. However, the value of "Benemid" in this respect has not yet been fully established, and it, too, may occasionally cause gastro-intestinal irritation.

INH appears to be the least toxic of the three principal antituberculous agents. (The isopropyl derivative has been abandoned as too toxic.) Side-effects are largely due to disturbance of the central nervous system—twitchings, dizziness, constipation, drowsiness, dryness of the mouth, urinary (bladder) retention, nausea, morning disturbance of vision, headache (aggravated by ephedrine or any vasoconstrictor) and rarely tinnitus and psychosis.

In the case of children with a tendency to convulsions, anticonvulsant medication should be given simultaneously with INH. INH should also be used prudently when there is any evidence of peripheral neuritis. There have been very rare instances of toxic effects on the hæmatopoietic system and liver. Dr. Middlebrook, of the National Jewish Hospital, Denver, advises that iron or vitamin B should not be given with INH, as these substances antagonize its therapeutic effect.

General Considerations.

In the chemotherapy of tuberculosis it is important to keep the patient under close supervision, so that the earliest signs of any toxic manifestation may be recognized. These demand cessation of the treatment, the administration of antihistamine medication, and often desensitization, especially in the case of PAS, by a gradu-

ally ascending system of dosage, beginning with very small amounts.

Blood counts and urine examination should be carried out once a month. Slight eosinophilia is not uncommonly found during streptomycin therapy, and any pronounced increase indicates the possibility of beginning intolerance.

Local Use.

Streptomycin, PAS and INH have all been used locally in different manifestations of tuberculosis. If pus is present, this should first be evacuated before the chemotherapeutic agent is injected. Streptokinase has been used as a liquefying agent.

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An acknowledgement is made to the Commonwealth Director-General of Health, Dr. A. J. Metcalfe, with thanks for permission to submit this paper for publication.

Addendum.

Since the above report was written the results of the Medical Research Council investigation on "Isoniazid in Combination with Streptomycin or with P.A.S. in the Treatment of Pulmonary Tuberculosis" have been published (*Brit. M. J.*, November 7, 1953). These showed that over a period of three months PAS (sodium) 20 grammes daily plus isoniazid 200 milligrammes daily "is a very effective combination of drugs, both clinically and bacteriologically; it ranks with the most efficacious treatment so far studied—namely, streptomycin 1 g. daily plus isoniazid 200 mg. daily and streptomycin 1 g. daily plus PAS (sodium) 20 g. daily". The report concludes:

A supplementary clinical comparison of all the 219 patients on streptomycin plus isoniazid and all the 172 on P.A.S. plus isoniazid confirms the clinical efficacy of combining P.A.S. with isoniazid. However, patients on streptomycin plus isoniazid gained a little more weight, and a higher proportion showed substantial radiographic improvement.

A preliminary analysis of results of sensitivity tests on each of the four treatments shows that P.A.S. (sodium) 10 g. daily plus isoniazid 200 mg. daily may prove to be a bacteriologically effective combination for at least three months. On the other hand, treatment with streptomycin 1 g. twice per week plus isoniazid 200 mg. daily is apparently less effective than streptomycin 1 g. daily plus isoniazid 200 mg. daily in preventing the development of bacterial resistance to isoniazid over a three-month period.

ALCOHOLISM.¹

By S. J. MINOGUE,
Sydney.

THIS paper is based on the experiences gained by ten years' association with thousands of alcoholics, who at one time or another have become interested in Alcoholics Anonymous. It thus has the great advantage of looking "from the inside out", not from "the outside in". The non-alcoholic sees only the bottle; the alcoholic wonders why he cannot drink like normal people.

For about 95% of drinkers alcohol is no problem. Their drinking is a matter for their own conscience, for theologians, and occasionally for the medico jurist. It is not one *per se* for doctors as doctors.

About 5% of drinkers become problem drinkers. Only two classifications of these drinkers are realistic: (i) the hard drinkers, who have their drinking more or less under control; and (ii) the dipsomaniacs or inebriates, who have no control over it at all.

The hard drinkers are those who drink too much. Fatigue, overwork, worry, ill health, pain, insomnia, or just a bad habit may start their drinking. But whatever

its cause, in time the patient complains of increasing mental and physical fatigue. The fatigue causes him to drink more to overcome it, and a true vicious circle is set up. It may be present from the beginning and be the real cause of his drinking. More often, however, it begins subtly after years of drinking, and persists for months after the patient has become a teetotaler.

The fatigue is genuine. The slightest mental and physical exertion becomes difficult. The patient becomes irritable and restless, loses confidence, and may become suspicious of others. The condition is usually associated with a loss of tolerance for alcohol. The man who once could drink comfortably two bottles of whisky a day becomes drunk after one or two beers. Once tolerance to alcohol is lost I have never known it to be regained.

If we study these patients over a long period we shall notice increasing dryness of the skin, due to vitamin deficiency. Alcohol is replacing meals, destroying vitamins *in vitro*. There is also a gradually increasing redness of the face with dilated venules; the liver becomes more and more palpable; the blood pressure, whilst remaining normal for a long time, becomes higher and higher—a systolic reading of over 200 millimetres of mercury and a diastolic pressure of 120 millimetres or more are common. The patient complains of morning vomiting, of tremulousness of the fingers, especially in the mornings, of gastric discomfort, and sometimes of hæmatemesis. Glycosuria is common.

The alcoholic history given by the patient is that he drinks mostly at nights and during the week-ends. He misses little or no time from work; he does not hide alcohol; and only towards the end does he take it home. Up to a point his drinking habits are but an exaggeration of those of the normal drinker.

Now if the patient gives up alcohol and is put on large doses of vitamins, in the vast majority of cases his health improves dramatically. The liver returns to its normal size; the blood pressure returns to normal; the skin becomes moist, and the glycosuria disappears. The condition is common in alcoholics, but I have seen no reference to it in the literature. Only when the condition has become chronic and the advanced classical signs of cirrhosis of the liver and such like have become pronounced do references to it appear in text-books. The syndrome described above seems to be known only to those who are interested in the treatment of alcoholics and see large numbers of them.

Why a normal drinker drinks too much is open to many interpretations. It may be a psychological escape from worry, pain and difficulties. For it is true that *in vino veritas*—if any man gets drunk sufficiently often, he forms his own pattern of drunkenness, which is reproduced exactly each time he gets drunk. The pure man when sober may become amoral whilst drunk. Many are guilty of homosexual crimes, of stealing, of burglary, and of other offences only when they are under the influence of alcohol. If they become teetotalers they do not offend again.

But why do only a small proportion of drinkers become pathological drinkers? Some "two bottles of whisky a day" men live healthily to more than three score years and ten. Others who drink far less develop the physical symptoms described above or Korsakoff's syndrome. Why? Why do some heavy drinkers, mostly in their forties, lose control of their drinking and within a few short weeks become true dipsomaniacs? We walk in a virgin field about which incredibly little is known. But it seems to me that there must be some link with the general fatigue, irritability and lack of tolerance to alcohol seen in so many ex-prisoners of war from Japan. Whilst it is true that some of these have hookworm infestations, dysentery and other tropical diseases, in many of them nothing abnormal can be found. Have they an unknown form of hepatitis associated with some unknown vitamin deficiency? I do not know.

On the other hand, the dipsomaniacs have a compulsion to drink enormous quantities of alcohol in a relatively short period of time. They may limit their drinking for a time, but sooner or later a bout is inevitable. Each patient has

¹ Read at a meeting of the New South Wales Branch of the British Medical Association on December 10, 1953.

his own pattern of drinking. He may go for weeks, months or years between bouts. He may drink moderately between bouts. The bout itself may last only a few hours; it may be prolonged for weeks. The uncontrolled drinking may be apparent from the first drink, no matter at what age it is taken; it may come on after years of heavy drinking. Once established, the bouts follow a pattern for each patient. But they tend to increase in severity, with shorter intervals between them with the passing of the years.

In dipsomania we have a condition very different from that found in heavy drinkers. The heavy drinker has no great compulsion to drink, and he can drink normally if he wants to. But the dipsomaniac is in the grip of something he cannot control. The heavy drinker may become an inebriate; the inebriate can never become a controlled drinker. For him there is no half-way house.

All members of Alcoholics Anonymous have experimented with themselves at one time or another to see if they can drink normally. They have tried to limit their drinks to so many a day; to drinking beer instead of spirits; to not drinking before a certain time of the day; to eating and drinking at the same time; to going off alcohol for weeks, months, or years. No matter what they did the end result was always the same. Many of them are well-known and successful business and professional men with a will of iron in business, and yet despite every effort of their will they could never drink normally. As many of them had been reared never to admit defeat, cost what it might, they set out to prove to themselves and others that they had their drinking under control. Only when they had lost everything and were destitute were many of them prepared to admit that alcohol had them beaten.

Most inebriates show definite mental and physical characteristics. They usually have intelligence, ability and driving force out of the ordinary. They can work long hours with great intensity for days, weeks or months, without much apparent effort. For these reasons many members of Alcoholics Anonymous are famous professional and business men.

Because they can usually do things better than the average man, in their drinking days they become arrogant, supercilious, fault-finding and aggressive. Because no one takes them at their own value of themselves they become suspicious, resentful and full of self-pity, with a grudge against the world, and especially against their nearest relatives. Then gradually develops the well-known character of the true inebriate, with his pathological lying and anti-social acts. He himself is right; all others are wrong. Unless he himself is prepared to admit that alcohol has become a problem to him, and he is anxious to do something about it, it is futile to talk to him about his alcoholism.

However, the main characteristic of the true inebriate is his compulsion to drink. Once he tastes alcohol he is powerless to stop himself from drinking, and verily in the words of Alcoholics Anonymous literature: "Without Divine help there is no adequate defence against that first drink." We have here a true irresistible impulse—despite the opinion of so many authorities that irresistible impulses exist only because they are not resisted.

The cause of their compulsion to drink is unknown, but most intelligent members of Alcoholics Anonymous realize that they have a great physiological need for fluids and carbohydrates. They will drink tea or coffee in large quantities without adequately satisfying their thirst. They are passionately fond of sweets and use abnormally large quantities of sugar in their food. At first some of them have a low blood sugar level with glycosuria. In later stages the blood sugar level rises and its curve may be a diabetic one. The number of inebriates who are being treated for diabetes surprises one.

A normal drinker can often conceal the smell of alcohol in his breath by the use of chlorophyll and such like, but the true inebriate after a few drinks reeks of alcohol, and, try as he may, he cannot conceal its smell. The alcohol is excreted through the skin, and in the course

of time the skin develops a peculiar dry texture, which is recognizable by touch, and which is almost diagnostic of alcoholism. Whilst this dryness may be partly due to the avitaminosis present, I have seen it only in alcoholics.

After a drunken episode a normal drinker is repelled by the sight and smell of alcohol. But the inebriate on the other hand is so tremulous and apprehensive that he must have alcohol before he can pull himself together. He seems to have an acute stimulation of his sympathetic nervous system, which is quietened by alcohol and which in turn the alcohol increases—a strange paradox, for which we have no explanation.

The stimulation of the sympathetic nervous system explains many of the physical phenomena met with during a bout. The patient becomes increasingly nervous, tense, restless and sleepless. Now the strange thing is that this nervous tension is present for a day or two before the bout begins and it becomes so intense that the patient is unable to stop himself from having that first drink. Anything psychological, joy or sadness, that increases the tension will precipitate a bout. Hence the saying, "the alcoholic has an unholy genius for getting drunk at the wrong time".

As the bout goes on the patient becomes increasingly tense, restless and apprehensive. He is as a coiled spring, not to be trusted, unpredictable. His blood pressure increases; his liver enlarges; he becomes more tremulous; he does not eat; there is a peculiar characteristic smell in his breath—a smell in which the presence of acetone can often be recognized. Convulsions may occur; hallucinations are present in the later stages. Unconsciousness and death may end the story.

We have here a syndrome for which we have no adequate pathological explanation. Only very occasionally apart from alcoholism, when toxic factors are suspect, as occurs in some of the psychoses associated with child-bearing, do we see such a condition. In it physical and psychological symptoms are bound indissolubly together. The fact that the symptoms are rapidly cured in most patients by the exhibition of insulin or adrenal cortex would indicate that some still unexplained glandular dystrophy is present.

Even when the patient recovers from the acute attack, usually during the third week, he has a violent reaction, when he becomes as tense, restless and depressed as he was before. Why this happens is still a mystery. After the third week he improves mentally and physically. He looks better, his blood pressure usually falls to normal, his liver becomes normal in size, and he is less tired than he was. Then in many cases during the third month a loss of weight occurs; he looks haggard and drawn; he is tense and very depressed. The temptation to drink becomes so great that the majority of subjects succumb to it. This physical condition in its turn passes off after some weeks and he begins to improve again mentally and physically. But often in the months to follow he has unexplained attacks of great mental and physical fatigue, which may last for weeks. Impotence may exist for many months after he gives up alcohol.

The more one analyses the problem of inebriacy, the more convinced one becomes of one's ignorance of the subject. We are walking in an unexplored virgin field. We know but a few isolated facts, parts of a jig-saw puzzle, with many pieces missing. The key to the problem is still unknown. If we realize this, we can see how futile is psychiatric treatment, such as shock treatment, "Antabuse", and psychotherapeutic procedures. We are dealing with a medical and not with a psychiatric disease. Even Alcoholics Anonymous does not cure the condition. All that it does is to teach the patient a philosophy of life which enables him to live without alcohol and without that tension which precipitates a bout. If he gives up this philosophy even after years of living it, his tension returns and his bouts return more severely than ever.

The problem of alcoholism is ever with us. Let us look at it as doctors and not as moralists and philosophers. Its victims are sick men and women to be treated; they are not moral lepers to be cast aside and preached at.

THE EFFECTS OF PROLONGED ALCOHOLIC EXCESS.¹

By JAMES ISBISTER,
Sydney.

CHRONIC ALCOHOLISM may be defined as a state of physical or mental invalidity produced by prolonged intake of excessive ethyl alcohol in its various forms. Dr. Minogue has dealt with the mental and social aspects of chronic alcoholism, and I propose to confine myself entirely to a consideration of the physical diseases produced.

Patients Studied.

This paper presents the clinical analysis of 86 patients admitted to general medical wards at Prince Henry Hospital, Sydney, under my direct care, over a period of four years commencing in January, 1950, and ending at the present time. All patients were admitted to hospital because they were physically ill, and none were admitted

The evidence of prolonged alcoholic excess was obtained in some cases from the patient, but this source of information was often unreliable. Confirmatory evidence was often obtained from relatives or friends, and in a few instances the condition was assumed on circumstantial evidence. Any analysis of the type of alcoholic beverage would have been quite unreliable.

Patients were practically all of the hospital class, so that an analysis of their occupations showed most to belong to the artisan and unskilled classes, especially the latter. Such an analysis would have no relevance in relation to the population as a whole.

Most patients showing physical effects of chronic alcoholism also had evidence, direct or indirect, of inadequate nutrition. Dietary histories under these circumstances are notoriously unreliable; but the general pattern was "no breakfast, a small lunch consisting of sandwiches, and a small dinner of meat and vegetables".

By the time these patients left hospital they had practically all been fully acquainted with the aetiology of

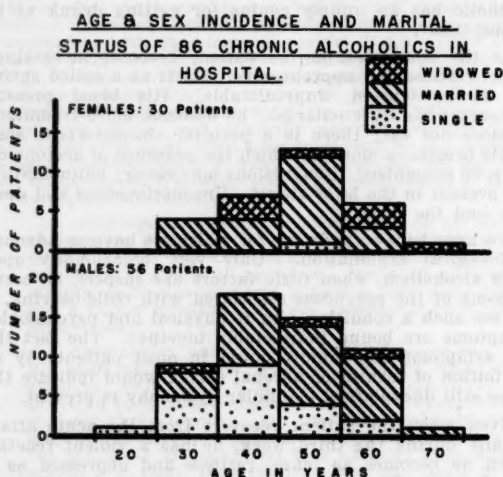


FIGURE I.

for the treatment of chronic alcoholism as such. The group is entirely unselected, most of those admitted having been recommended directly by general practitioners to an "acute" general hospital. A similar unselected group in recent medical literature could not be found for comparison. A group of 78 cases of chronic alcoholism described by Joske and Turner (1952), of Melbourne, is selected, as the studies were carried out in a research unit investigating particularly gastro-intestinal and liver diseases.

In the present series no attempt is made to analyse in detail dietetic or social histories, laboratory studies or autopsy findings. The information is compiled from routine ward clinical notes written by resident medical officers and some notes of my own added to these. Most emphasis is placed on the final diagnosis with some mention of separate symptoms in a few conditions.

The incidence of chronic alcoholism is difficult to determine, as many sufferers are treated in out-patient departments or are admitted to psychiatric institutions. Others again do not seek or require hospital treatment. The present 86 cases have been selected from approximately 5000 admissions, and include only cases in which prolonged alcoholic excess was the sole or major cause of illness. There were other cases in which chronic alcoholism coexisted with another separate disease, the latter being the cause of the patient's admission to hospital. These latter patients are not included, so the apparent incidence of chronic alcoholism is a conservative figure.

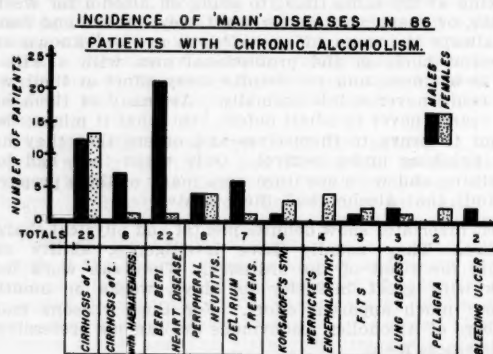


FIGURE II.

their condition. Most patients stated their sincere intention to abstain from alcoholic beverages; but one wondered in most cases how long most of these promises would last. However, it can be said that the only readmissions were amongst those patients who had permanent pathological changes, such as cirrhosis of the liver. The total number of readmissions, which number is not included in the total, was six.

The clinical analysis of this group of patients is presented in simple fashion, graphically where possible, and no attempt has been made at any statistical analysis. The conclusions drawn are therefore those which appear reasonable and which would probably prove statistically significant in a group of this size.

Age, Sex and Marital Status.

Figure I shows the age, sex and marital status of the 86 patients. The ratio of males to females was 2:1, there being 56 males and 30 females. The average age of the males was forty-seven years and that of the females fifty-two years. This difference is probably not significant. Figures in relation to marital status show a high number of bachelors and an almost complete absence of spinsters. The high proportion of widows to widowers is apparent, though less striking.

Incidence of "Main" Diseases.

The term "main" disease signifies the main syndrome caused by chronic alcoholism. In some cases two or more syndromes might coexist, but in the majority one predominated. The patient is then classified under the predominating disease. The total number shown in Figure II is 88, the additional two being cases of cirrhosis of the liver in which peripheral neuritis was also a major clinical feature. The main points in this analysis, apart from

¹ Read at a meeting of the New South Wales Branch of the British Medical Association on December 10, 1953.

cirrhosis of the liver and beriberi heart disease, which will be discussed separately, seem to be as follows: (i) male predominance among patients with *delirium tremens*; (ii) female predominance among patients with peripheral neuritis, Korsakoff's syndrome and Wernicke's encephalopathy; the only two cases of pellagra occurred in women.

In three instances of peripheral neuritis difficulty was experienced in differentiating the condition from thallium poisoning in a person already suffering from chronic alcoholism. The neuritic symptoms are very similar.

The four patients with Wernicke's encephalopathy presented with confusion, ophthalmoplegia and sometimes nystagmus. This condition is due to thiamine deficiency

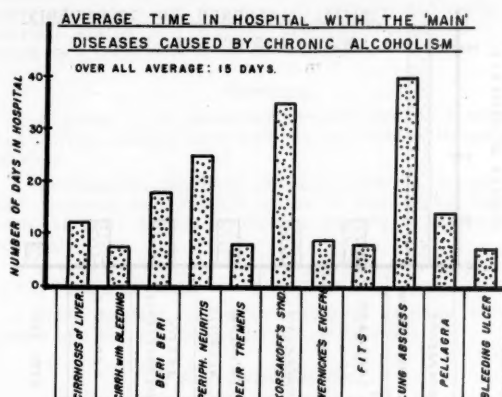


FIGURE III.

and is sometimes referred to as cerebral beriberi. The only other conditions which will be analysed further are cirrhosis of the liver and beriberi.

Average Stay in Hospital.

Figure III illustrates the average period spent in hospital for the "main" diseases. The short period for cirrhosis of the liver is due to the high death rate and also to the fact that some patients were treated palliatively by aspiration of ascitic fluid only. The overall average of fifteen days for the 86 patients gives an entirely false idea of the total period of disability. Most patients had been incapacitated for a few weeks before their admission to hospital. It was also the policy to discharge patients from hospital as soon as they could be cared for at home, or at a "non-acute" hospital or institution. Very few patients would have been fit for their ordinary occupation within a week of discharge from hospital.

Deaths.

There were 13 deaths, seven among males and six among females (see Figure IV). This gives a considerably higher mortality rate amongst females than males. All deaths were due to cirrhosis of the liver, except one which was due to beriberi heart disease. This latter death, curiously enough, occurred in the single case of beriberi heart disease in a female.

Cirrhosis of the Liver.

From Table I the following facts appear to be significant: (i) Cirrhosis of the liver without bleeding from oesophageal varices has a higher incidence in females than in males. (ii) Cirrhosis of the liver with bleeding from oesophageal varices has a higher incidence in males than in females. (iii) The mortality among patients with bleeding from oesophageal varices is higher than among those without such bleeding. (iv) The overall mortality of both sexes is the same.

Figure V illustrates some of the facts of Table I in graphic form, but also shows the large proportion of single men in the group of male alcoholics who develop cirrhosis

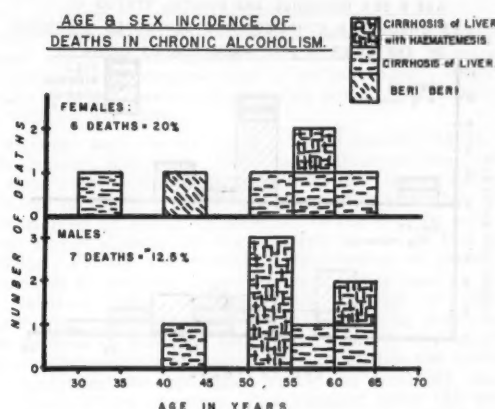


FIGURE IV.

of the liver both with and without bleeding from oesophageal varices.

Beriberi Heart Disease.

The incidence of beriberi heart disease in Sydney is probably much higher than one would expect, or than some would admit. I have no doubt about the diagnosis in these cases, though the severity of the symptoms varied. Figure VI illustrates the age and sex incidence and marital status. There were 22 cases, a total incidence of 26%; 21 of these patients were males, giving an incidence in males of 37%. Beriberi heart disease was therefore as common in males as all forms of cirrhosis of the liver (34%). The age distribution is similar to that of male alcoholics as a whole. The number of single men is not significant as with cirrhosis of the liver.

The main clinical features of pure beriberi heart disease in this group are due to predominant failure of the right ventricle and are as follows: (i) a thiamine-deficient diet taken for two months or more; (ii) almost complete confinement of the condition to males; (iii) dyspnoea on exertion, and weakness; (iv) dependent oedema; (v) some evidence of peripheral neuritis; (vi) cyanosis; (vii) little or no orthopnoea; (viii) increase in venous pressure; (ix) enlarged liver; (x) low diastolic blood pressure and high pulse pressure (water-hammer pulse); (xi) warm extremities; (xii) enlarged heart with sinus rhythm;

TABLE I.

Sex.	Total Number of Patients.	Cirrhosis of the Liver without Hematemesis.		Cirrhosis of the Liver with Hematemesis.		Cirrhosis of the Liver (All Cases).	
		Cases.	Deaths.	Cases.	Deaths.	Cases.	Deaths.
Male	56	12 (22%)	3	7 (12%)	4	19 (34%)	7
Female	30	13 (43%)	4	1 (3%)	1	14 (47%)	5
Total, both sexes	86	25	7	8	5	33	12

(xiii) absence of rales at the lung bases; (xiv) absence of evidence of other aetiology. These clinical features agree closely with those described by Blankenhorn *et alii* (1946). The characteristic clinical picture is that of a middle-aged man admitted to hospital with cardiac failure, lying flat in bed, with a considerable degree of cyanosis of the face; familiarity with this picture makes "spot" diagnosis fairly reliable.

Of this group of 22 patients, eleven were admitted to hospital with congestive cardiac failure, the exact cause of which had not been determined. An adequate history and examination revealed the cause as beriberi, without the

Cases of beriberi heart disease vary from the florid picture described above of predominant right ventricular failure to one with considerable left ventricular failure as well. The latter type occurs mainly in the older age group and is probably related to some degree of pre-existent ischaemic heart disease. The florid form therefore occurred in the younger patients and the less typical form in the older ones.

Those patients, particularly in the older age group, who had had beriberi heart disease, either repeatedly or in a mild form, for some time often developed a permanent limitation of cardiac reserve.

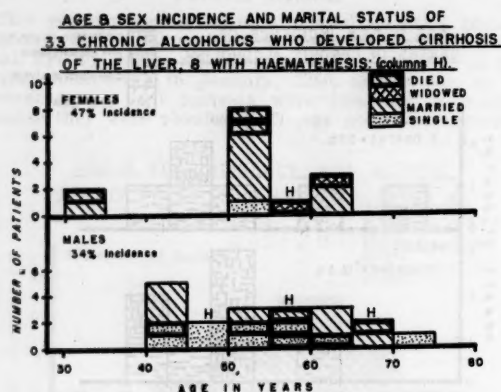


FIGURE V.

need for special investigation. Figure VII shows the initial diagnosis in 22 cases, and it will be noted that in only one case was the patient admitted to hospital with the correct diagnosis. It is interesting to note the patients admitted to hospital as suffering from aortic incompetence

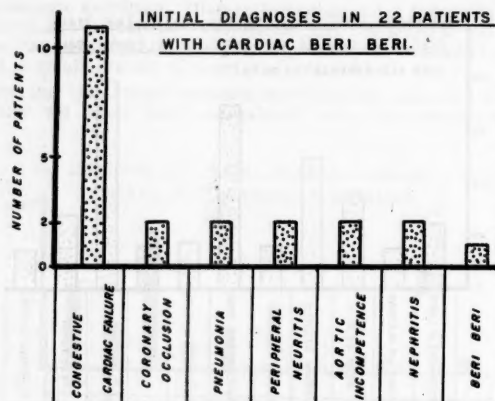


FIGURE VII.

Figure VIII shows the distribution of cases in six-monthly periods over the four years. Most of the really typical cases in the younger patients occurred from July, 1951, to July, 1952. At this point there was an almost

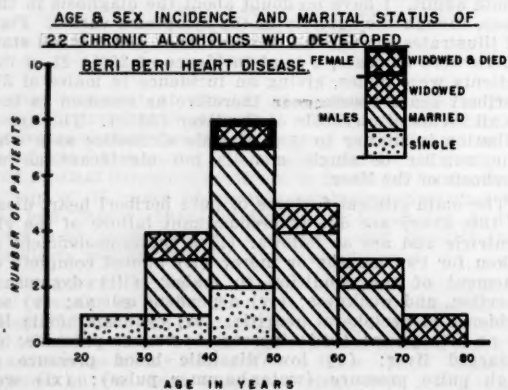


FIGURE VI.

and nephritis; the former diagnosis was made because of a large pulse pressure felt at the radial pulse, the resident medical officer then convincing himself that he could hear an aortic diastolic murmur. Nephritis was diagnosed because of the gross oedema without much shortness of breath. This clinical syndrome is unknown to many in the medical profession, and this fact undoubtedly accounts for much incorrect treatment. It is also thought that the true nature of this syndrome is overlooked because the patient with congestive cardiac failure is admitted to hospital and treated with digitalis and mersalyl, and recovers, mainly on account of the thiamine content of the ward diet.

INCIDENCE OF BERI BERI HEART DISEASE IN CHRONIC ALCOHOLICS DURING SIX MONTH PERIODS FOR 4 YEARS.

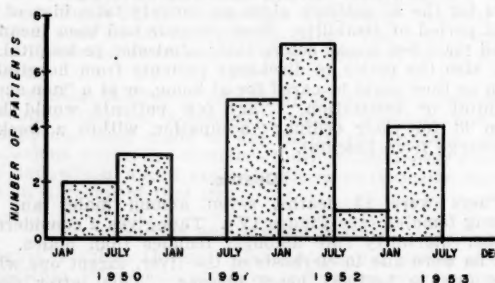


FIGURE VIII.

abrupt cessation of the typical case, and most that have occurred since have been less acute and in the older age group. The reason for this is not evident, but it may be related to economic conditions.

Comment.

Certain facts seem to emerge from this clinical analysis of a group of unselected chronic alcoholics. Bachelors form a significantly large proportion of the males, especially those with cirrhosis of the liver. Widows form a less noticeably high proportion of the females. Cirrhosis of the liver is the commonest disease caused by chronic alcoholism, females being especially liable to cirrhosis without portal

hypertension and males contributing the majority with portal hypertension.

Beriberi heart disease is a relatively common condition and is confined almost entirely to males. It also appears to have a periodic incidence. Peripheral neuritis, Korsakoff's syndrome and Wernicke's encephalopathy are conditions in which females predominate. Lung abscess should be considered in all cases of pneumonia occurring in alcoholics.

The causes of these differences with regard to sex, marital status and the disease syndrome produced are not clear. Undoubtedly constitutional differences in the two sexes are partly involved. However, it is thought that the clue is probably in the dietary intake. If really reliable dietary histories could be obtained in all cases there might be some correlation between the type of dietary deficiency, sex, marital status and disease syndrome produced. This could be a fruitful field for investigation.

Summary.

1. A group of 86 unselected chronic alcoholics admitted to a general hospital have been studied from a clinical point of view.
2. Information has been produced showing the age and sex incidence and marital status of this group, together with the main clinical syndromes leading to admission to hospital.
3. A study is made of the average period in hospital and of the causes of death.
4. More detailed studies are made of patients with cirrhosis of the liver and beriberi heart disease.

Acknowledgements.

The General Medical Superintendent of the Prince Henry Hospital, Dr. C. J. M. Walters, has given permission for publication of the information relating to these patients. The work of the nursing staff and resident medical officers of the hospital in caring for these patients and in assisting with this survey is appreciated.

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THE CALCULATED RISKS OF CHEMOTHERAPY.¹

By DAVID F. GRAY,

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Melbourne.

It is becoming increasingly evident that it is not sound medical practice to weigh the undesirable effects of chemotherapy and chemoprophylaxis against the undisputable benefits and to discount them as unfortunate but unavoidable corollaries.

Modern medicine demands that the practitioner should be familiar not only with the antibacterial spectrum of different antibiotics, but also with their selective toxicity, their action on the normal body flora, and their ability to sensitize human beings. He must be acutely conscious of the causes and consequences of the emergence of drug-resistant strains. This knowledge will assist him in selecting the antibiotic of choice, in its use either therapeutically or prophylactically and, by minimizing misuse, in reducing the calculated risks to their proper perspective.

It is proposed to deal with these problems from the viewpoint of a bacteriologist, and I shall attempt to set

out, as far as they are known, the conditions most likely to bring about these undesirable effects and to suggest from these reasonable control measures. To this end I shall deal with them in order of increasing importance.

Selective Toxicity.

It is not necessary to discuss in detail here the toxic manifestations which may be encountered; these are recorded in detail by Finland and Weinstein (1953).

Provided the possible toxic effects of a drug are known, it then becomes a problem of assessing these against the risk to the patient of withholding chemotherapy or the prophylactic use of the drugs.

Microbial Imbalance.

The production of a microbial imbalance is likely to occur whenever antibiotics are employed for therapeutic or prophylactic purposes over a period, though, especially with the broad spectrum group, this period may be as short as four or five days.

Bierman and Jawetz (1951), David Smith (1952), and Finland and Weinstein (1953) have discussed this problem at some length. The term "superinfection" is now generally applied to the development, during chemotherapy, of an infection by an organism resistant to the drug in use. The most likely explanation for this lies in one of two possibilities. Firstly, the successful suppression of a sensitive organism in diseased tissue leaves the way open to direct or indirect cross infection from carriers or patients harbouring resistant strains. In theory, at least, much can be done to minimize this risk. Secondly, the microbial balance normally maintained by competition for available nutrients and for biological space and probably also by antibiotic action of some kind, ranging from the simple production of hydrogen peroxide to more complex metabolites, becomes upset at the site of action of the drug. The result of suppressing sensitive strains is an abnormal multiplication of resistant forms such as monilia, klebsiella, pseudomonas or resistant staphylococci. Simple pruritus, oral thrush, vesicular stomatitis or pulmonary or intestinal monilia infections are not uncommon after the use of broad spectrum antibiotics for more than a few days. Finland and his colleagues refer to staphylococcal pneumonia arising in this way, and to acute, sometimes fatal, staphylococcal enteritis, and Meier (Annotation, 1953) records similar enteritis in patients given terramycin pre-operatively.

Dr. William Gilmour, of Perth, recently recorded six cases of fulminating septicaemia due to resistant staphylococci occurring as a complication of influenza, all fatal in twenty-four hours.

A further complication of prolonged chemotherapy usually attributed to suppression of intestinal bacteria is vitamin deficiency, particularly of the B complex. While it is true that intestinal bacteria are capable of synthesizing vitamins in the bowel, recent work by Judith Cregan and Dr. Nancy Hayward of this department (1953) has reopened the question. The small intestine normally carries only a transient flora, chiefly of oral, Gram-positive species, and no evidence was obtained that either folic acid or thiamin could be absorbed from the gut below the level of the ileo-caecal valve (Hayward and Harrison—to be published). Therefore there is some doubt as to the validity of the claims that chemotherapy may be responsible in this particular manner for vitamin deficiency.

The logical solution to this interference with the normal body flora would appear to be as follows: (i) to observe every available means of suppressing cross infection with resistant strains; (ii) to assess critically the potential benefits of chemoprophylaxis, either as a long-term project in, for example, the suppression of recurrences of rheumatic fever or of streptococcal infections generally, or, as a short-term pre-operative or post-operative measure; (iii) to discontinue the use of chemotherapeutic lozenges for trivial infections of the oro-pharynx or for any other purpose.

¹ Read at a clinical meeting at the Royal Melbourne Hospital, November 1, 1953.

Drug Hypersensitivity.

It is now clear that sensitization of persons to chemotherapeutic agents is a relatively common occurrence, not only in patients receiving the drugs, but also in persons concerned with their manufacture and preparation for therapeutic use. This subject was discussed in THE MEDICAL JOURNAL OF AUSTRALIA of July 25, 1953, under "Current Comment", and dealt with in detail in a report from the Ministry of Health (1953).

As with allergic reactions generally, sensitization is most likely to follow single or repeated contacts with small amounts of the drug, which stimulate only a trivial antibody response. Therefore, full courses of systemic treatment would be less likely to cause trouble than relatively superficial contacts. The figures available support this; for example, sensitization follows topical application of penicillin in 10% to 15% of cases. The Ministry of Health report records 256 cases in which hospital staff members had become sensitive to antibiotics through handling them in their work, including up to 5% of nurses, and I understand that Dr. E. R. H. Clarke, of the Commonwealth Serum Laboratories, is undertaking a study of workers in the penicillin plant to determine the extent of sensitization occurring there. The obvious portals of entry of the drug in these cases are the skin and the mucous membranes of the mouth, the respiratory tract and the eye. The contact could be direct, or from droplets suspended in the air during the adjustment of syringes, from contaminated dust, or possibly from steam issuing from an autoclave.

Although a severe reaction to one antibiotic is often accompanied by sensitivity to others, an allergic tendency on the part of the subject does not appear to be a necessary condition. Naturally, some people are more prone than others to sensitization, but there is a belief that all will become sensitized in time. Thus, while some cases have resulted from the first or second contact, others have appeared only after five years of continuous association with antibiotics. Streptomycin and penicillin were the commonest sensitizing agents in the British survey; but other antibiotics have been incriminated also, as might be expected on general immunological grounds.

The clinical manifestations of sensitization are described in detail by Finland and Weinstein. They vary widely from a simple skin reaction with or without fever, through angioneurotic oedema, asthma and "drug fever" or serum sickness type reactions, to death from anaphylactic type shock. Pick and Patterson (1953), mention six fatal cases in America and three in England. If therapy is not stopped, the symptoms of patients receiving chemotherapy tend to increase in intensity with successive doses.

Some sensitized nurses are reported to respond to simple treatment and brief avoidance of the antibiotic; others have been able to resume work if adequately protected with masks, goggles and gloves; but in a large proportion even remote contact with the drug is intolerable, and there are in this category many who have had to abandon nursing as a profession. Claims for successful desensitization are conflicting, and it would seem that the chances of success in this direction are of the same order as with similar conditions due to other sensitizing agents. In patients undergoing chemotherapy the use of antihistamines, the cessation of therapy and the promotion of excretion are indicated, while according to Finland and Weinstein, ACTH and cortisone may be helpful or even life-saving.

In assessing cases of hypersensitivity it is important that consideration be given to the possible role of some other sensitizing agent, such as common drugs, antiseptics, cosmetics or procaine. Control of this risk is a problem of management which is lessened by a knowledge of contributing factors.

1. The use of antibiotics should be strictly limited to infections within their expected range of action.

2. Lozenges, dusting powders, skin ointments and oily suspensions for topical application are contraindicated unless the drug is given systemically at the same time.

3. Gowns, masks, gloves and preferably goggles should be worn during the handling of drugs, every care being taken to avoid contact with skin or mucous surfaces, and contamination of the preparation site. These precautions have been found in practice to reduce, but not apparently to abolish, the risk of sensitization (Ministry of Health report).

4. Steam issuing from autoclaves is suspect in the case of heat-stable drugs.

5. Air should be expelled from syringes while the needle remains in the container. Preferably the same needle should be used for inoculating as for withdrawing the dose, as it has been shown that, contrary to the common belief, careful insertion of a needle through a rubber cap up to 50 times does not cause undue blunting of the point.

6. The allergic history of the patient should be ascertained and intradermal sensitivity tests before the use of the drug are a wise precaution. Suction before injection will guard against the accidental administration of drugs by the intravenous route, which is far more likely to produce a state approaching anaphylaxis than either intramuscular or subcutaneous injection. It is considered time well spent to keep patients under observation for at least five to ten minutes after injection in case of a delayed reaction.

The Emergence of Drug-Resistant Strains.

By far the most serious challenge to the continued usefulness of chemotherapy, the emergence of drug-resistant strains, is a risk that can be attributed only in part to the misuse of chemotherapeutic agents. Fortunately, the ability to develop multiple drug resistance with comparative ease has been observed in few pathogens, and it is with these that we are chiefly concerned at the moment; these include *Staphylococcus pyogenes*, *Mycobacterium tuberculosis* and *Haemophilus influenzae*. With other genera (streptococcus, neisseria, shigella, klebsiella and so on), resistance does arise, but the rate at which it occurs is as yet not alarming. However, it seems probable that under existing conditions most organisms are likely to be able to utilize this protective mechanism to a variable degree in the fight for survival.

The literature during the last two years has carried a very large number of papers dealing particularly with the "hospital staphylococcus" and resistant tubercle bacilli, and it is neither necessary nor possible in this discussion to quote them in detail. However, it is convenient to use the staphylococcus to illustrate this argument, and the figures of Clarke, Dalglish and Gillespie (1952) show clearly how far this organism has progressed along the road to complete immunity to our most effective antibiotics. These workers recovered resistant staphylococci from ward air and dust, as well as from the nasal swabs of patients and staff. They found the highest incidence of multiple resistance in wards where antibiotics were used most freely. Of 199 strains isolated throughout the hospital, 22% were resistant to penicillin, sulphonamides, streptomycin and the broad spectrum antibiotics, while in two wards this figure reached 28%. In the casualty department, on the other hand, none of 40 strains isolated showed resistance to more than two of the drugs, though 37 were resistant to penicillin.

Figures of local origin make it clear that the position in Victorian hospitals has not yet deteriorated to the same extent. At the Alfred Hospital it is still possible to treat 25% of staphylococcal infections with penicillin, and whereas the number of strains resistant to other drugs has increased in the past two years, only 4.6% have proved resistant to all (Tolhurst, 1953).

In a recent survey of the staff and patients of a suburban hospital with an outbreak of staphylococcal infection in infants, we found that of 22 strains in patients and contact carriers, all were resistant to penicillin and three to streptomycin. In the Public Health Laboratory, routine staphylococcus isolations in the past six months, apart from those just quoted, amounted to 40 strains, all from a non-hospital environment. Of these, 50% were resistant

to penicillin, 17% to streptomycin and 12% to aureomycin. Of interest in this discussion was the high incidence in this group of strains showing partial resistance to terramycin (33%) and aureomycin (65%). This may indicate the shape of things to come outside the hospital environment.

The final figures I wish to present were supplied to me by Dr. Gilmour (1953). He found that from 1946 to 1950, in Perth, the response of osteomyelitis to penicillin was dramatic. The average duration of chemotherapy was only two weeks and 48 out of 60 patients showed rapid and full recovery. From 1951 to 1953, however, only three out of 13 patients showed this response to penicillin. Penicillin either failed in the rest or was not used because of adverse drug resistance tests. However, other antibiotics were used, both the broad spectrum group and streptomycin in some cases, but the response was never as dramatic as in the early series. In 10 out of 13 cases recovery was slow and incomplete, and there was multiple involvement with gross bone destruction. Gilmour considers that we are now dealing with a new type of osteomyelitis, not unlike that of the pre-penicillin days, and the evidence he produces would appear to support this view.

I should like to consider briefly at this stage the possible origin of drug-resistant strains. Why, for example, is the position so much worse in the hospital environment than in general practice? It is improbable that antibiotics are administered with less care or on less justifiable grounds in the hospital. There is, however, far greater opportunity for cross infection to occur once resistant strains have emerged, and here, in part at least, appears to lie the explanation. Therefore, to argue that the position in Melbourne with regard to fully resistant staphylococcal strains is not serious is highly dangerous, because once these forms appear, the only barriers to their dispersal are those we can erect against cross infection, and in practice these have proved to be disappointing.

The actual mechanism of the development of drug resistance will not be clearly understood until we know more about the mode of action of the different chemotherapeutic agents, and it is certainly not the same for all organisms. The important fact is that while some strains admittedly possess a natural resistance, many are capable of acquiring resistance when exposed to sublethal doses. Whether the latter condition operates by selection of mutant forms, normally suppressed by sensitive forms better equipped to survive, or by actually stimulating mutation, is not of great importance from the practical point of view. What is important is to recognize those practices most likely to lead to the exposure of pathogens to sublethal doses, because it is on these practices that the conversion of sensitive to resistant forms largely depends.

While some of these are already widely recognized, others perhaps are not so obvious; they include the following: (i) Topical application leading to poor penetration. (ii) Failure to maintain an adequate blood level for a sufficient period of time. (iii) Failure of an antibiotic reaching adequate blood levels to diffuse in sufficient concentration through diseased tissues or past natural barriers. This is probably a major factor in, for example, the emergence of resistant strains of tubercle bacilli. (iv) The handling of chemotherapeutic agents, which has been shown to produce conditions conducive to the development of hypersensitivity—namely, repeated small doses reaching the skin or mucous membranes. There would appear to be every reason to suppose that such conditions, coupled with the high nasal and skin carrier rate of *Staphylococcus pyogenes* in hospital personnel (30% to 90%), would also stimulate the emergence of drug-resistant strains.

Suppression of Drug Resistance.

Of these factors the first two, being widely appreciated, should no longer present a serious risk; but the failure to secure adequate contact of the drug with all the organisms present because of poor diffusion is less easily overcome. It may be lessened by attacking the lesion from every possible angle: in infections of mucous membranes

systemically and topically; in pulmonary lesions, such as tuberculosis, systemically and by inhalation. Another useful practice is the rational use of drug combinations and rotational régimes of the type found effective in suppressing the rate of emergence of resistance in tubercle bacilli, for example (i) streptomycin for three weeks with PAS, (ii) isoniazid for three weeks with PAS, followed by a further course of streptomycin with PAS, *et cetera*.

When drug-resistant strains are encountered either in patients or in staff, their potential point of attack should be carefully examined in the laboratory, and they should be hit hard, the newer antibiotics such as magnamycin or ilotycin or suitable combinations of other antibiotics being used in an effort to eliminate them. However, the difficulty of overcoming the carrier state, either by chemotherapy or by any other means, is well recognized. In such cases the use of carefully prepared autogenous vaccines may be worthy of consideration.

The final problem of the risk of carriers handling antibiotics will need to be approached in the manner discussed for the reduction of sensitization. We are faced at the present moment with an increasing incidence of drug-resistant pathogens of several types. If every effort is made to minimize the emergence of fresh resistant strains, then the emphasis will fall on controlling cross infection, particularly in hospitals, and on endeavouring to destroy resistant strains whenever they are reported by the laboratory or are detected by failure of the expected clinical response.

Conclusions.

The risks associated with the increasing dependence on chemotherapy as a means of controlling infectious disease, of which the most alarming is the emergence of drug-resistant strains, are slight compared with its benefits. Careful consideration of the problems involved shows that much can be done to keep these risks in their true perspective. It is noteworthy that the preventive measures suggested are the same for more than one undesirable effect of chemotherapy in several instances, as, for example, with hypersensitivity and the development of drug-resistant strains in carriers. This tends to simplify the precautions that are clearly necessary.

If adequate steps are not taken, however, it seems likely that the ratio of benefit to risk may become narrowed to such an extent that we may find ourselves drifting back towards the pre-antibiotic era, as is certainly happening with the "hospital staphylococcus". It is probably only a question of time before the rate of discovery of new antibiotics fails to keep pace with the increasing facility with which strains already resistant to one or more drugs are able to develop resistance to new antibiotics, and although this outlook may seem unduly pessimistic in the light of the continued benefits of chemotherapy, it cannot be lightly disregarded.

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Reports of Cases.

A FATAL CASE OF CHRONIC SALMONELLA TYPHIMURIUM SEPTICÆMIA: THE INTRAVENOUS USE OF CHLORAMPHENICOL.

By A. W. VENABLES, M.D., M.R.A.C.P., and
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ILLNESS due to infection with salmonella organisms falls into three patterns. Enteritis, acute septicæmic states producing illnesses like typhoid fever, and milder more prolonged septicæmic states leading eventually to localization of infection all occur. The site of any localization is variable. Such diverse conditions as meningitis, osteomyelitis, urinary tract infection, cholecystitis, breast abscess, empyema and pericarditis have all been reported as complications of salmonella infections of various types other than *Salmonella typhi*.

In the case presented below, recurrent suppurative cervical adenitis due to *Salmonella typhi-murium* was associated with prolonged low-grade septicæmia, which terminated after eighteen months with widespread suppuration within the reticulo-endothelial system.

Clinical Record.

X., a female child, aged two years, was admitted to the Children's Hospital, Melbourne, on May 16, 1951. Since infancy she had been with foster parents. Her neonatal history was unknown, but since then she had had no significant illness. Seven weeks prior to her admission to hospital she had developed a lump in her neck, which was not obviously painful, but which enlarged rapidly. When she was examined in the out-patient department, the lump appeared to be a suppurating cervical gland. Pus was obtained on incision, and from this salmonella was grown in pure culture. This organism was identified as *Salmonella typhi-murium* by the Public Health Laboratory, Bacteriology Department, University of Melbourne. A course of chloramphenicol was given, but a further gland abscess developed, again requiring incision.

On her admission to hospital, the patient was a small, somewhat pale child (her hæmoglobin value was 72%, 10.4 grammes per 100 millilitres), weighing just over 18 pounds. There were sinuses over both anterior triangles of the neck from which pus was discharging. She had patches of thrush on her tongue, as had been noted on her first visit to the out-patient department, but there was no other clinical abnormality. Sensitivity tests (disk technique) showed the organism (*Salmonella typhi-murium*) to be sensitive to streptomycin (one microgramme per millilitre) and to chloramphenicol (five microgrammes per millilitre), but to be resistant to aureomycin (five microgrammes per millilitre). A similar organism was obtained from blood culture on her admission to hospital. The serum agglutinin titre to salmonella Group B "O" was one in 320. *Salmonella typhi-murium* was grown on culture from the stool on her admission to hospital, and then intermittently until her death.

The sinuses healed after the provision of adequate drainage for the abscesses in her neck, splinting, the local application of ultra-violet light, and a course of streptomycin (150 milligrammes every six hours given intramuscularly for fourteen days). Her general condition improved with a gain of one pound in weight, but irregular fever (temperature up to 100° F. daily) persisted. She was discharged home on June 15, 1951.

One week later she was readmitted to hospital, when a blood culture taken prior to her discharge yielded a growth of *Salmonella typhi-murium*, sensitive as before to streptomycin and chloramphenicol and resistant to aureomycin.

She appeared well, although the pyrexia was still present. Her neck was healed and no other physical abnormality was found. Intramuscular injections of streptomycin (150 milligrammes every six hours) combined with the oral administration of chloramphenicol (250 milligrammes every six hours) was given for fifteen days. Her fever persisted, and culture from the blood continued to yield *Salmonella typhi-murium*. The organism isolated after this latest course of chemotherapy was found to have developed resistance to at least 10 microgrammes per millilitre of streptomycin, but was inhibited by chloramphenicol in a concentration of two microgrammes per millilitre (it resisted one microgramme per millilitre), as determined by the serial tube doubling dilution technique. All subsequent sensitivity tests were performed by this method. There was no clinical evidence of any focus for the bacteriæmia, and the child appeared well, and made a slow but definite weight gain.

Massive doses of chloramphenicol (500 milligrammes every three hours) were then given orally for twenty-one days. During this time tonsillectomy and adenoidectomy were performed because of the persistent presence of salmonella in throat swabs. Even this massive dosage of chloramphenicol did not affect the pyrexia. There were no side effects. Bacteriological assay of her serum for chloramphenicol on the sixth day of this course revealed no inhibition of growth of the salmonella or of an equally sensitive staphylococcus in a serum dilution of one in two. Further attempts at eradication of the infection were therefore temporarily abandoned, and the child was discharged from hospital on August 20, 1951.

She remained well and active, gaining weight steadily, until November, when further suppurative cervical adenitis developed, necessitating her admission to hospital for incision. At this time there was a rapid deterioration in her health, with a loss of four pounds in weight in three weeks. The organism now obtained was found to be inhibited by chloramphenicol in a concentration of two microgrammes per millilitre (it resisted one microgramme per millilitre), inhibited by terramycin in a concentration of two microgrammes per millilitre (it resisted one microgramme per millilitre), and only moderately resistant to streptomycin (it resisted 3.9 microgrammes per millilitre, and was inhibited by 7.8 microgrammes per millilitre).

The child's general condition was then poor, and severe anæmia was present, her hæmoglobin value being 52% (7.5 grammes per 100 millilitres). Diffuse monilial stomatitis was found, and *Salmonella typhi-murium* was still present in the pharynx. The liver edge was just palpable. Heart and lungs were normal. The anæmia was corrected by blood transfusion, and in view of the clinical condition chemotherapy was again given, admittedly without much prospect of success. Chloramphenicol (250 milligrammes) and terramycin (125 milligrammes) were given by mouth every three hours. On the eighth day of this course bacteriological assay of her serum failed to reveal effective concentrations of either antibiotic. The salmonella and the staphylococcus grew readily in undiluted serum and in all serum dilutions from one in two to one in 16. On the tenth day of the course chemotherapy was discontinued. The fever persisted, but her neck gradually healed, her general condition improved, and her weight rose to 22 pounds 10 ounces. In view of this spontaneous improvement she was again discharged from hospital on January 5, 1952.

She remained well, apart from recurrent monilial stomatitis, until April, when cervical adenitis again recurred together with a moderate degree of anæmia, but no loss of weight (her weight was then 24 pounds six ounces). On her readmission to hospital abscesses on both sides of her neck required incision. Throat swab, stool, pus and blood all yielded cultures of *Salmonella typhi-murium*, now resistant to two microgrammes per millilitre of chloramphenicol, but sensitive to four microgrammes per millilitre. She was given a blood transfusion, but the anæmia recurred and her neck was slow in healing. Her temperature rose from previous levels to swing to 102° F. daily, and her general condition gradually deteriorated.

* In receipt of a grant from the National Health and Medical Research Council.

In view of the results of previous oral therapy, chloramphenicol was on this occasion given intravenously. The solution was prepared by dissolving 2.5 grammes of chloramphenicol per litre of 0.25 isotonic saline with 5% glucose in infusion flasks and sterilized by being autoclaved for fifty minutes at a pressure of 10 pounds per square inch (115° C.). Bacteriological assay showed no change in potency after sterilization.

Chloramphenicol was given in a dose of 2.5 grammes daily, involving an intake of one litre of fluid by continuous intravenous infusion every twenty-four hours. This was continued for fourteen days. There was a good deal of phlebitis and periphlebitis, but no other untoward reaction.

The temperature fell dramatically to normal. The neck wounds began to heal more rapidly and swabs from them and from the throat became "negative". *Salmonella* (sensitive to two microgrammes per millilitre of chloramphenicol) persisted in the stools, together with other organisms sensitive or moderately sensitive to chloramphenicol, and for this reason a short oral course of chloramphenicol was given overlapping the end of the intravenous course. (The other organisms were a streptococcus, sensitive to four microgrammes per millilitre, coliform bacilli, sensitive to eight microgrammes per millilitre, and a *Staphylococcus albus*, sensitive to 32 microgrammes per millilitre.)

Bacteriological assay of serum on the third day of the intravenous administration of chloramphenicol showed complete inhibition of growth of the patient's organism in a serum dilution of one in 24. The calculated chloramphenicol concentration was between 96 and 128 microgrammes per millilitre of serum.

Soon after cessation of therapy the temperature returned to its original level (up to 100° F. daily). The salmonella gradually reappeared in culture from the various sites, the blood culture result becoming positive fourteen days after the cessation of intravenous therapy. However, the child made general improvement and was sent home on July 9, 1952, after three months in hospital.

She was readmitted once again on July 21, 1952, with recurrent adenitis and anaemia. Local treatment of the abscess and blood transfusion were repeated, but from then on her condition remained poor. Three weeks after her admission to hospital she developed intermittent abdominal pain, for which no adequate cause was found. The anaemia recurred, and after blood transfusion she was given a further short intravenous course of chloramphenicol (1.5 grammes daily for six days). Her temperature again fell, but there was little other effect. Signs developed at the base of the left lung suggestive of collapse of the lower lobe, and a chest X-ray examination revealed elevation of the left side of the diaphragm. The liver became palpable one to two fingers' breadth below the right costal margin, and the abdomen was noted to be full in contrast to the general wasting, but no other definite signs could be elicited. On September 20 the left subphrenic space was extensively needled to exclude subphrenic abscess. A small amount only of blood-stained fluid was obtained. This was found to contain pus cells, and from it *Salmonella typhimurium* was grown on culture. Her condition progressively deteriorated, and hard mobile masses were felt in the lower part of the abdomen. Laparotomy on October 4 revealed many suppurating glands within the abdomen. Death occurred on October 9.

Necropsy Findings.

Necropsy (performed by Dr. J. W. Perry) revealed enlarged suppurating lymph glands in the neck and mediastinum, and within the abdominal cavity, where many mesenteric glands were involved. There was a large abscess in the spleen, which was adherent to the diaphragm. Patchy basal pulmonary consolidation was present. The heart was normal. No abnormality was found in the central nervous system. There was gross inflammatory change in the colon, caecum and appendix, and in the terminal part of the ileum, with hyperplasia and extensive

ulceration of the lymphoid tissue. The liver and bile duct system were normal.

Notes on Bacteriological Technique.

A modification of the filter paper disk technique for penicillin determination described by Vincent and Vincent (1944) was used in initial sensitivity tests. Blotting paper disks nine millimetres in diameter were saturated with solutions of each antibiotic in appropriate concentration, and placed on the surface of freshly inoculated blood agar plates. After sixteen to twenty hours' incubation zones of growth inhibition were compared with zones obtained in control tests with standard organisms.

More accurate in-vitro sensitivity tests were performed by the serial tube doubling dilution technique. In this test the basic medium was "Difco" tryptose broth in two millilitre volumes with an inoculum of one drop (33 drops per millilitre) of six-hour broth culture diluted one in 10. The tube containing the lowest concentration of antibiotic in which there was no macroscopically evident turbidity after sixteen to twenty hours' incubation was taken as the end point.

The serial tube dilution technique was also employed for assay of autoclaved chloramphenicol solution, by the use as test organisms of the patient's salmonella (resistant to two microgrammes per millilitre, sensitive to four microgrammes per millilitre) and a strain of *Staphylococcus aureus* (resistant to one microgramme per millilitre, sensitive to two microgrammes per millilitre). In this test the inoculum of *Staphylococcus aureus* was one drop of a six-hour broth culture, whilst the inoculum of *Salmonella typhimurium* was as used above. The use of this doubling dilution technique revealed no deterioration in the autoclaved chloramphenicol solution.

The assay of serum for chloramphenicol was performed by the serial tube dilution technique. Serum obtained whilst the patient was on oral therapy revealed a level of less than two microgrammes of chloramphenicol and of terramycin per millilitre; the patient's organism grew readily in her undiluted serum. Serum obtained during the intravenous administration of chloramphenicol showed a level of approximately 96 microgrammes of chloramphenicol per millilitre, which corresponded to inhibition of growth of the patient's organism by a one in 24 dilution of her serum.

Discussion.

Systemic salmonella infection is an unusual phenomenon, but, as has already been stated, may lead to meningitis, osteomyelitis and other focal lesions. In the case reported the primary feature was recurrent suppurative cervical adenitis, associated with a persistent salmonella infection in the pharynx and bowel. The same organism was also present in the blood intermittently throughout the course of the illness. The oro-pharyngeal infection was associated with monilial stomatitis. Despite the evidence of persistent bowel infection, diarrhoea was present on two occasions only. There was a mild and brief episode about the middle of the illness, and severe diarrhoea with melaena occurred just prior to death. The inflammatory lesions present in the bowel at necropsy appeared from this evidence to have developed terminally. Death occurred primarily as the result of extensive suppuration in the spleen and lymph glands throughout the body. Gall-bladder infection was not a contributory factor in the persistent bowel infection.

There was no evidence of bacterial endocarditis, either on clinical examination or at necropsy. The septicæmia must therefore have been related to the persistent foci in either the bowel or the neck, but the underlying mechanism is difficult to explain.

There was evidence from the serum assays that chloramphenicol and terramycin given even in massive doses by mouth produced no significant blood levels. One must assume that there was defective absorption of these drugs. Intravenous administration of chloramphenicol produced high blood levels, but even then failed to eradicate the

infection permanently, although it produced a temporary clinical response. Intravenous administration of chloramphenicol in saline solution by the technique described (suggested by the representatives of Parke, Davis and Company, as other preparations were not available), proved free of complications other than phlebitis. This technique may well prove useful in other infections in which chloramphenicol is indicated, but oral administration is impracticable, or when there is evidence of impaired absorption of antibiotic from the bowel.

In this case there was evidence that an effective bowel concentration of chloramphenicol was not produced by intravenous administration of the drug.

Very large total doses of chloramphenicol were given to this child, but no evidence of bone marrow depression was noted. Anæmia did recur throughout the illness, but was closely correlated with gland suppuration, and developed only with the latter. Platelets and granular leucocytes were never reduced in number. Bone marrow biopsies were not performed.

With no direct evidence regarding the mechanism of production of the septicæmia, and in the absence of lasting response to the high levels of chloramphenicol presumably maintained in the serum, it is impossible to suggest any means by which the ultimate development of widespread metastatic lesions and consequent death could have been avoided.

Summary.

A case is presented of recurrent suppurative cervical adenitis due to *Salmonella typhi-murium*.

During the course there was persistent infection of the alimentary tract together with a fairly constant blood-stream involvement.

Evidence was obtained showing failure of oral antibiotic therapy to be due to poor intestinal absorption of chloramphenicol and terramycin, but establishment of adequate serum concentrations of chloramphenicol by intravenous administration failed to eradicate the infection.

Death occurred after eighteen months from widespread suppuration in lymph glands and spleen, together with gross enteritis.

Acknowledgements.

We wish to thank Dr. V. L. Collins and Dr. J. W. Perry for help and advice in the management of the patient and in the preparation of the paper.

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Notes on Books, Current Journals and New Appliances.

Family Doctor. Published monthly by the proprietors, the British Medical Association, Tavistock Square, London, E.C.1. Sole agents for Australia and New Zealand: Gordon and Gotch (Australia), Limited. Subscription for twelve months: 20s. (sterling), including postage.

DOCTORS who subscribe to *Family Doctor* will find that they will want to read a good deal of it themselves before they part with it for the benefit of their patients, or even of their family. The February, 1954, issue is no exception. Articles of general interest deal with the growth-promoting power of antibiotics when fed to animals, a school for boys from a difficult home environment, the usual collection of interesting facts under the heading "Close-up of Science", and a description of "Invalid Kitchens", a service which provides meals at low cost for invalids in England. Then there are articles about twins, influenza, phenobarbitone, children with asthma, coronary thrombosis, the definition of madness, the third of Walter Alvarez's three articles on "How to Live with your Nerves", and a number of articles

primarily of family interest on babies, teenagers and food. Altogether, a large quantity of sound material is presented with an attractiveness and originality that will give almost universal pleasure, a statement that can be fairly made about any monthly issue of *Family Doctor* that has appeared up to date. Any doctor who would like a free sample copy of *Family Doctor* to be sent to him is invited to send his request to the Editor of THE MEDICAL JOURNAL OF AUSTRALIA.

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"Review of Physiological Chemistry", by H. A. Harper, Ph.D.; Fourth Edition; 1953. Los Altos, California: Lange Medical Publications. 10" x 7", pp. 338, with many diagrams. Price: \$4.00.

The first edition appeared in 1939.

"The Year Book of Pediatrics (1953-1954 Year Book Series)", edited by Sydney S. Gellis, M.D., and Isaac A. Abt, M.D.; 1953. Chicago: The Year Book Publishers, Incorporated. 7½" x 5½", pp. 436, with many illustrations. Price: \$6.00.

One of the "Practical Medicine Series of Year Books".

"The Year Book of General Surgery (1953-1954 Year Book Series)", edited by Everts A. Graham, A.B., M.D., with a Section on Anesthesia edited by Stuart C. Cullen, M.D.; 1953. Chicago: The Year Book Publishers, Incorporated. 7½" x 5½", pp. 590, with many illustrations. Price: \$6.00.

One of the "Practical Medicine Series of Year Books".

"The Surgical Clinics of North America"; 1953. Philadelphia and London: W. B. Saunders Company, Melbourne: W. Ramsay (Surgical), Limited. Nationwide Number. 9" x 8", pp. 324, with 117 illustrations. Price: £6 per annum in paper binding and £7 5s. per annum in cloth binding.

This is a "Nation-Wide Number". It comprises, first of all, a symposium on ambulant surgery consisting of twelve contributions with a foreword. This is followed by a section of seven articles dealing with seven subjects.

"Aids to Inorganic Chemistry", by R. G. Austin, B.Sc. (Lond.), F.R.I.C.; Second Edition; 1953. London: Baillière, Tindall and Cox. 6½" x 4", pp. 480, with 22 illustrations. Price: 10s. 6d.

One of the well-known "Students' Aids Series".

"The Thyroid: A Physiological, Pathological, Clinical and Surgical Study", by T. Levitt, M.A., F.R.C.S. (Eng.), F.R.C.S. (Ed.), F.R.C.S.I.; 1954. Edinburgh and London: E and S. Livingstone, Limited. 10" x 7½", pp. 630, with many illustrations, some in colour. Price: £5 5s., postage abroad 2s. 6d.

Intended for everyone interested in thyroid dysfunction.

"Ulcerative Colitis and its Surgical Treatment", by Bryan N. Brooke, M.Chir., F.R.C.S.; Foreword by F. A. R. Stammers, C.B.E., T.D., B.Sc., Ch.M., F.R.C.S.; 1954. Edinburgh and London: E. and S. Livingstone, Limited. 10" x 7", pp. 158, with many illustrations, some in colour. Price: 37s. 6d., postage 1s. abroad.

Intended for physician and surgeon alike.

"Planning Guide for Radiologic Installations", by the Committee on Planning of Radiologic Installations of the Commission on Public Relations of the American College of Radiology, Wendell G. Scott, M.D., Chairman; 1953. Chicago: The Year Book Publishers, Inc. 10½" x 7½", pp. 352, with many illustrations. Price: \$8.00.

This is a joint endeavour by radiologists, representatives of companies manufacturing X-ray equipment and film, Federal health agencies, the American Hospital Association and the American Institute of Architects.

"Human Neuroanatomy", by Oliver S. Strong and Adolph Elwyn; Third Edition; 1953. London: Baillière, Tindall and Cox. 10½" x 7", pp. 494, with 357 illustrations. Price: 57s. 6d.

This is "an attempt to link structure and function into dynamic pattern without sacrificing anatomical detail".

The Medical Journal of Australia

SATURDAY, MARCH 6, 1954.

All articles submitted for publication in this journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words or phrases.

References to articles and books should be carefully checked. In a reference the following information should be given without abbreviation: surname of author, initials of author, year, full title of article, name of journal without abbreviation, volume, number of first page of the article. If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

THE PROGRESS OF OPHTHALMOLOGY IN AUSTRALIA.

ADVANCES in any of the branches of medicine are often the result of the researches of one individual. Sometimes, as we all know, the individual who receives the credit has merely placed a coping stone on a structure which has been elaborated over a period of years by many different persons. In these advances medical societies and associations often take a large part, and in Australia we may say of ophthalmology that a great deal has been accomplished already by the Ophthalmological Society of Australia (British Medical Association) since its inauguration in March, 1938. At its last annual meeting in Adelaide in October, 1953 (12 have been held since the first in 1939), Dr. Darcy Williams gave a comprehensive review of the activities of the society; indeed, he traced its history in some detail and named individual ophthalmologists who had contributed new knowledge. The Ophthalmological Society of Australia (the "O.S.A." as it is sometimes conveniently called) has consistently maintained a high standard at its annual meetings. These were suspended temporarily during the war, but that was only to be expected. One of the methods adopted by the society has been to secure the presence at the meeting of one or more distinguished ophthalmologists from overseas. Such well-known figures as Ida Mann, Aaron Green, Sir P. C. Livingston, Henrik Sjögren, Arthur Lister, F. B. Walsh, J. H. Doggart, T. K. Lyle, John Foster, A. B. Reese, H. Weve and Seymour Philips have come to this country and have inspired Australian ophthalmologists and spurred them on to further efforts. One of the earliest visitors, Dr. Ida Mann, who was Professor of Ophthalmology in the University of Oxford, has since made her home in

Australia and is doing work of the greatest value in Western Australia. One of the early actions of the society was to set up a research and scientific committee, with J. Ringland Anderson, of Melbourne, as convener. The terms of reference of this committee were very wide, and amongst other things included proposals for investigation into the cause of blindness. In its endeavours to investigate the causes of blindness the society was not successful, because a request in 1939 to the National Health and Medical Research Council for a grant to investigate the incidence of blindness met with refusal. It was quite obvious, of course, that while the causes of blindness were being investigated its incidence should be determined. It has remained for ophthalmologists in Tasmania to make surveys on their own account. The findings of Norman Gregg in regard to the effect on the fetus of rubella occurring in the mother during her pregnancy were first reported at a meeting of the Ophthalmological Society. Those who were privileged to be present on that occasion will not readily forget the effect which Gregg's communication had on the meeting. This is not the place in which to set out the original work which has been reported at annual meetings of the society; space would not permit this. It must suffice to state that the work has been of a consistently high standard and that the *Transactions* of the society have earned for themselves a high reputation. The last annual meeting in Adelaide was in some respects an epoch-making occasion, because it was then that the formation of the Ophthalmic Research Institute of Australia was announced. The Ophthalmological Society had been trying for some years to establish a research institute, but had difficulty on account of the fact that it wished to have donations made to its fund to be allowable as deductions for income tax purposes. It was learned in 1950 that in order to create such a fund it would be necessary to establish a new institution, a registered company for preference, which would be accepted by the Minister for Health as "an approved research institute". Certain technical difficulties had to be overcome, and eventually the Director-General of Health was able to announce that he had approved of the institute as "an approved research institute". This approval has been acknowledged by the Commissioner for Taxation. The Ophthalmic Research Institute of Australia was incorporated in the Australian Capital Territory on October 30, 1953. The objects for which the institute is established are the following:

1. The name of the Company is "The Ophthalmic Research Institute of Australia".
2. The objects for which the Institute is established are:
 - (a) To conduct and carry out research study and investigation of and into the nature structure and functions of and relating to the human eye as a means of seeking to discover the nature origins and causes of affections and diseases of and relating to the human eye and as affecting human vision,
 - (b) To seek and discover the origins and causes of blindness in man by the application of any or all of those branches of science which are relevant to this purpose and to make the best use of knowledge so gained for the improvement of means for the prevention of blindness in man,

- (c) To conduct and carry out such research study and investigation by the application of all or any relevant branches of science including ophthalmic medicine, ophthalmic surgery and allied sciences in all their branches,
- (d) To promote conduct or assist in the promotion or conduct of research in all matters conditions affections or disorders with which the science or profession of ophthalmology is concerned,
- (e) To use or cause to be used knowledge acquired as the result of research study and investigation for the improvement or means for the prevention or treatment of affections and diseases of and relating to the human eye and/or affecting human vision,
- (f) To apply for purchase or otherwise acquire any patents brevets d'inventions licenses concessions and the like conferring any exclusive or non-exclusive or limited right or any secret or other information as to any invention which may seem capable of being used for any of the purposes of the Institute or the acquisition of which may seem calculated directly or indirectly to benefit this Institute and to use exercise develop or grant licenses in respect of or otherwise turn to account the property rights or information so acquired and to apply for or otherwise acquire any trade marks copyrights and designs and the like and to use exercise develop and otherwise turn to account any property or rights so acquired,
- (g) To use all such means as may be deemed advisable for the conduct of research study and investigation including the acquisition of real and personal property by purchase lease exchange hire or otherwise and the founding setting up equipping maintaining and subsidising of hospitals laboratories offices buildings plant equipment and apparatus,
- (h) To acquire any rights or privileges which the Institute may deem necessary or convenient for the purposes for which it is established,
- (i) To establish and maintain a museum for the installation viewing and study of specimens relating to ophthalmological research,
- (j) To acquire maintain and equip a scientific library relating to ophthalmology and medical science allied thereto and to extend improve and add to the same,
- (k) To conduct courses of research study instruction and teaching for and of members of the medical profession engaged in ophthalmological research including the delivery of lectures and the provision or arranging of demonstrations clinical surgical medical or otherwise,
- (l) To disseminate information knowledge or advice relating to ophthalmological research by such means as the Institute may deem advisable including printed publication or otherwise and with a view thereto to acquire set up maintain print publish and circulate magazines journals circulars pamphlets or other scientific compositions or works,
- (m) To found or aid in the founding of ophthalmological research foundations or scholarships by itself or in conjunction with any hospital or other research institute or organization with objects similar to the Institute and to make and pay grants or moneys to persons engaged in ophthalmological research,
- (n) To employ officers and servants in connection with any of the objects of the Institute and to pay such sums and retiring allowances or provisions to such officers and servants as may be deemed necessary or desirable,
- (o) To subscribe or guarantee money for any purposes connected with the objects of the Institute or calculated to further the same and to co-operate or amalgamate with any association organization or institute formed for purposes connected with the objects of the Institute,
- (p) To enter into and perform agreements with any hospital corporation institute or person or body of persons for any purpose connected with the objects of the Institute,
- (q) To obtain funds and to accept any gift endowment devise or bequest made to the Institute generally or for the purpose of any specific object and to accept and carry out any trusts attached to any such gift endowment devise or bequest,
- (r) To sell improve manage develop exchange lease mortgage dispose of turn to account or otherwise deal with all or any part of the property and rights of the Institute,
- (s) To borrow raise or secure the payment of money in such manner as the Institute may think fit and in particular by mortgage of all or any of the Institute's property the issue of debentures or debenture stock perpetual or otherwise charged upon all or any of the property or rights of the Institute both present and future and to purchase redeem or pay off any such securities,
- (t) To invest and deal with the funds moneys or property of the Institute not immediately required,
- (u) To draw make accept endorse discount execute and issue cheques promissory notes bills of exchange warrants debentures and other negotiable or transferable instruments,
- (v) From time to time to make rescind or alter such by-laws not being inconsistent with the Memorandum of Association or with the Articles of Association of the Institute for the time being in force for the regulation of any of the affairs or purposes of the Institute as may be deemed necessary desirable or convenient,
- (w) To do all such other things acts and matters as are incidental or conducive to the attainment of the above objects or any of them.

These objects have been set out in full so that there may be no misunderstanding by members of the medical profession about the organization. The research funds of the institute will be kept "as a special fund" and payments

from this fund will be made on the advice of the research committee. Scientific members of the institute will include medically qualified investigators and also graduates in science specializing in physiology, physics and so on. Members of the institute will probably wish to become members of the Ophthalmological Society of Australia, and there are ways and means for this to be possible under the by-laws which deal with the formation of special groups of the British Medical Association.

There is no doubt that the Ophthalmological Society of Australia has made a great step forward, and one which eventually will, it is hoped, achieve advances and add to the scientific knowledge of the world. Beginnings have to be made, and although this beginning may be small, it will, guided and controlled in a wise manner, advance from strength to strength. At the annual meeting of the society in October last Professor Weve, of Utrecht, than whom there is no more famous and erudite ophthalmologist, in replying to the toast of his health, made a speech which produced a profound effect on all those who heard it. It was a speech which should have been broadcast to every scientific worker in this country. Professor Weve declared that the greatness of a people was not measured by the size of its country or by the number of its inhabitants or by the strength of its armed forces or by the might of its labour unions or by its material wealth and prosperity. All these might be of great help, and under many circumstances might be necessary. The real greatness of a nation depended on its *élite* of heart and mind, an "aristocracy" that might be found in every section of the community. He pointed out that a militarist and athletic Sparta had left no lasting mark on the map of human civilization, but that the spirit of Athens was still alive and active in all parts of the world which had any culture at all. Indeed, he declared, the great saints, the great philosophers, the great scientists and the great artists were those who had created throughout the ages the centres of culture and human progress. He thought that the day might come and might even not be so very far away in which the torch of civilization, held for many centuries in such a high and gallant fashion by the peoples of Europe, would have to pass into other hands, and it might well be that the countries in the southern hemisphere like Australia would have to take it over. He implored Australians to be prepared for this task. Addressing his colleagues the ophthalmologists particularly, he bade them not to be content by showing to the world a corps of ophthalmic surgeons of high standing, but to try to take a lead in the development of ophthalmic science. He thought that the new institute which was to come into being might be the means through which ophthalmologists could make their contributions to the greatness of Australia. He referred to the immense amount of work which had been carried out in the London Institute of Ophthalmology, and he thought that much the same might be achieved in Australia perhaps on a more modest scale. He declared that Australia had the men, and he was convinced that they would find also the means. This imposed a moral duty on the society. These were noble words, and they were spoken with great intensity and conviction by one who was well qualified to utter them. When this new institute is launched Australians must see that success is assured.

Current Comment.

THE SURGICAL TREATMENT OF GASTRO-DUODENAL HÆMORRHAGE.

A WELL-KNOWN and competent Australian surgeon who died a year or two ago, on being told by a doctor friend that he was suffering from a duodenal ulcer, remarked: "I beg of you don't ever allow any of my surgical brethren to operate on your duodenum." This advice, by and large, was sound; but, of course, there are occasions on which it would be wrong. Every surgeon and every physician of experience can recall cases in which a life might have been saved if surgical operation had been undertaken, or if it had been undertaken at an earlier stage than it actually was. An interesting discussion has recently been published by Gordon Ferguson on the surgical management of gastro-duodenal hæmorrhage.¹ Ferguson deals with 17 cases in which he has performed operation at a small surgical centre in a period of fifteen months. He describes four types of management. The first type is ultra-conservative, in which operation is undertaken only as a last resort. The second type is that of selective surgical intervention. The third type is described as immediate operation. The fourth type is that of initial medical treatment and early operation if bleeding persists or recurs. Four of Ferguson's patients died, and three were aged over seventy years. It was not only their age which caused their deaths, because two other patients over seventy years of age were successfully operated on. Other factors were involved. One of the three patients over seventy years of age was submitted to the second type of treatment. After he had been operated on and partial gastrectomy had been performed, the wound ruptured and the patient died of pulmonary embolism. A second patient, aged seventy-six years, died of chronic pyelonephritis and myocardial disease three days after partial gastrectomy. A third patient, aged seventy-seven years, was unable to give a history, and it was questionable whether anything save partial gastrectomy held out any hope of recovery for him. At operation no ulcer was found, and gastrectomy was not performed. The patient died of continued bleeding, and an ulcer was found in the stomach at autopsy. Ferguson found that in his series one of the problems most difficult of solution was the maintenance of the elderly patients' condition after operation, when they should be relinquishing milk foods and be beginning to take solid diet. They seemed to lose all interest in food; the effort of feeding themselves was not, they felt, worth while, and they were lethargic, loath to eat and fickle of appetite. It required great skill and endeavour on the part of the nurses to tempt them to take even the smallest of the most tasty helpings. These patients had not been wearied by operation, but in Ferguson's opinion they had been wearied by a debilitating pre-operative illness, which he thinks was much more important. He holds that if this pre-operative period could be shortened by early operation, with consequent early cessation of hæmorrhage, the chance of recovery would be greater than it was with delayed operation or with conservative treatment. He thinks that there should be no hesitation in operating on a patient aged more than seventy years with proved ulcer or with a typical history. He states that what he writes about the elderly patient applies also to the patient with a concomitant medical lesion, especially angina of effort and coronary disease. Such a patient derives nothing but ill from recurrent hæmorrhage, even though transfusion replaces the lost blood. A low hæmoglobin level not only diminishes the nutrition of the myocardium, but also in his opinion increases the work required of it to keep the distant tissues adequately oxygenated. With each successive episode of bleeding the patient's condition deteriorates. Of the 17 patients, 11 were suffering from gastric ulcers. He therefore concludes that the confirmed presence of a gastric ulcer in a patient with hæmatemesis or with melæna is a consideration in favour of early operation.

¹ *Lancet*, January 30, 1954.

No ulcer was found at operation in four instances. He states that the correct procedure to adopt in such circumstances, together with the application of gastrotomy, is partial gastrectomy. In the final discussion on his cases, Ferguson states that the first type of management, that of ultra-conservative treatment, should more properly be called mismanagement and should no longer be tolerated. It is interesting to note that Ferguson admits that there is a growing realization that partial gastrectomy is not without its unpleasant sequelae, and that even apart from the various types of post-gastrectomy syndrome, it is questionable whether the "gastrectomized" patient is ever again quite the man he was. He thinks that blood transfusion is necessary when the haemoglobin value falls below 70%.

In relation with this paper it is interesting to read one by Emmanuel M. Rappaport.¹ Rappaport writes on the difficulties in the recognition of lesions of the stomach at operation by palpation and inspection. He reports five cases of recurrent bleeding from the upper gastro-intestinal tract. The site and the presumptive cause of haemorrhage were determined by radiography or gastroscopy in each instance before operation; yet at operation the surgeon was unable to corroborate the clinical results. In one case a hiatus hernia was repaired, and in another an area of antral gastritis was excised, while in three cases no cause for bleeding was found. Owing to recurrence of haemorrhage a second operation was required in each case, and then the original pre-operative diagnoses were confirmed. In four cases a second operation would have been unnecessary had the stomach been opened for inspection at the time when the pathological changes had been noted on radiography or gastroscopy. We may recall Ferguson's case in which no ulcer was found and partial gastrectomy was performed, but an ulcer was found at autopsy. Of course gastrectomy may have been performed without inspection of the interior of the stomach. Rappaport states that the errors of the types described by him usually occur when operation is performed after bleeding has stopped. These errors arise from several causes. More than one lesion may be present, and each of them may be a potential source of haemorrhage, and removal of one does not prevent recurrence of bleeding from the others. The commonest example is, he states, the recurrence of bleeding shortly after a total gastrectomy for duodenal ulcer when an undiscovered lesion had been left behind in the gastric stump. He states that there is no single or simple formula for the surgical management of cases of recurrent haemorrhage when radiographic and endoscopic studies repeatedly give normal results. He insists that radiological and gastroscopic findings must be substantiated, if necessary by opening the stomach. Rappaport refers to a report by Findley, Kirzner and Palmer of four cases of carcinoma of the stomach which were diagnosed correctly by radiography or gastroscopy, and yet at operation no lesion could be identified, and in three cases a second operation was required. He also refers to a report by Jankelson, in which repeated haemorrhage took place. The stomach was opened with negative findings, and yet at post-mortem examination a lymphosarcoma was found. We all know that even at post-mortem examination it may be extremely difficult to find a point from which bleeding has taken place if some time has elapsed between the haemorrhage and death.

THE PRODUCTION OF AMINO ACIDS UNDER POSSIBLY PRIMITIVE EARTH CONDITIONS.

ONE of the great difficulties in assessing the possibility of the spontaneous evolution of living things in the early stages of the earth's history is to account for the appearance of such organic compounds as amino acids before there were any living organisms. Stanley L. Miller, in a series of simple but effective experiments, has actually produced amino acids under conditions which might have existed at the time of the cooling of the earth to a temperature compatible with the existence of such sub-

stances.¹ It has been suggested that, at this time, the earth had an atmosphere of water, hydrogen, ammonia and methane, instead of oxygen, carbon dioxide, nitrogen and water as at present. This view has been supported by Oparin, by Urey and by Bernal.

The author constructed an apparatus to circulate a mixture of methane, ammonia, water and hydrogen past an electric discharge. The apparatus was a closed system with a flask in which water was boiled continuously, the steam mixing with the gases in another large flask, circulated past the electrodes, condensed and emptied back into the boiling flask. A U-tube kept the circulation in one direction. The apparatus was run continuously for a week. Towards the end the water in the flask became turbid from colloidal silica from the glass and reddish in colour owing to organic substances adsorbed on the silica. Mercuric chloride was added as soon as the apparatus was opened to prevent contamination with microorganisms. Some of the organic substances were removed by adding barium hydrate, others by boiling with sulphuric acid. The remaining solution was tested for amino acids by paper chromatography. This showed that a number of amino acids were present in the solution and glycine, α alanine and β alanine were definitely separated and probably aspartic acid and α -amino-*n*-butyric acid. Other amino acids were present, but in amounts too small for absolute determination. Other organic substances formed have not been investigated yet. The amounts of amino acids produced were very small, but this was only a preliminary experiment and the conditions were probably not optimal. The production of amino acids and other organic substances under conditions which might well have resembled those existing when the earth was cooling opens up large new fields for investigation and may bring us one step nearer to understanding the events which led to the development of life on this planet.

ZOONOSES.

AN important field in which the tracks of human and veterinary medicine cross is that of the zoonoses. Zoonoses, a relatively new term denoting diseases of animals transmissible to man, was the subject of a seminar arranged jointly by the World Health Organization and the Food and Agricultural Organization, and held in Vienna in November, 1952. The principal papers presented and summaries of the discussions have now been published in a World Health Organization monograph.² In an introduction to the monograph it is pointed out that more than 80 zoonoses have been listed, but in European countries perhaps 10 or 15 can be said to occupy a position of importance. The five diseases considered at the seminar—bovine tuberculosis, brucellosis, leptospirosis, "Q" fever and rabies—were selected for their broad interest to the countries of Europe. The section on bovine tuberculosis contains five papers: two of these (one by K. A. Jensen, of Denmark, and one from the Weybridge Veterinary Laboratory, Surrey, England) describe relevant laboratory techniques; another from the Weybridge Veterinary Laboratory deals with the preparation of purified protein derivative tuberculin; J. N. Ritchie, of the British Ministry of Agriculture and Fisheries, gives an account of the measures taken to control tuberculosis in British herds; a further paper by K. A. Jensen is concerned with its manifestations in man and in cattle. In the section on brucellosis, G. E. Renoux, of the Pasteur Institute, Tunis, considers aspects of the human form of the disease, and A. W. Stableforth, of the Weybridge Veterinary Laboratory, deals with control of the animal form; in another paper from this laboratory diagnostic techniques are described. The epidemiology of leptospirosis in the Italian rice fields is the subject of a paper by B. Babudieri, of the *Istituto Superiore di Sanità*, Rome; J. W. Wolff, of the Institute of Tropical Hygiene and Geographical Pathology, Amster-

¹ *Science*, May 13, 1953.

² "Advances in the Control of Zoonoses: Bovine Tuberculosis—Brucellosis—Leptospirosis—Q Fever—Rabies", World Health Organization Monograph Series, Number 19: 1953. Geneva: World Health Organization. 9½ x 6½", pp. 276. Price: 15s.

¹ *Ann. Int. Med.*, October, 1953.

dam, gives a comprehensive account, in two articles, of the methodology of leptospirosis research. Babudieri also contributes two papers to the section on "Q" fever; in one he outlines its epidemiology, diagnosis and prophylaxis, and in the other he makes detailed recommendations on laboratory diagnostic methods. M. M. Kaplan, of WHO, and E. C. Hulse, of the Weybridge Laboratory, report on the methods used and results obtained in a recent survey of the prevalence of "Q" fever in 28 countries. The final section of the monograph, that on rabies, opens with a comprehensive paper by Pierre Lépine, of the Pasteur Institute, Paris; he discusses the forms taken by natural and experimentally induced infection in the dog, outlines the development of antirabies vaccination and considers the value of treatment with hyperimmune horse serum. In a further paper Lépine reviews methods for the diagnosis of rabies. M. M. Kaplan analyses the basis of antirabies field control programmes and includes, as an annexe to his paper, a report by A. Zeissig on the control of rabies in foxes.

The papers were prepared with the knowledge that both administrative and laboratory workers would attend the meeting and so cover a wide range of interests. Just the same, as is explained in the introduction, it would have been impossible, within the time limits imposed, to prepare comprehensive reviews on each of the topics, and emphasis was therefore placed on highlights and recent advances in relation to each disease. The usefulness is pointed out of bringing together medical and veterinary workers to discuss topics of common interest, especially in the field of the zoonoses, where a combined medical and veterinary approach, in which the full resources of public health and agricultural departments are used, constitutes the most effective means of combating these diseases. It is stated that the prevention and eradication of zoonoses in human beings can be accomplished in large part by control of these diseases in animals; so that it is natural for public-health officials to give every assistance—moral, financial, scientific and educational—to agricultural authorities in carrying out programmes of animal-disease control. This can take such practical forms as the following: financial subsidies for control programmes; the fostering of research and epidemiological surveys in newly emerging problems such as those of "Q" fever and leptospirosis; popular education in control of rabies and hydatid disease. The task of agricultural and veterinary authorities lies in tracking down the source of infection, applying measures for control and eradication, cooperating in surveys, educating farmers and so on.

A great deal of technical information with stimulating comment from many authorities has been collected in this monograph. No doubt a partly different selection of zoonoses would be of greater interest in Australia (hydatid disease could certainly displace rabies), although two at least of those included (leptospirosis and "Q" fever) are of considerable local importance. However, that is not really the point, and it is to be hoped that the monograph will achieve here as elsewhere its primary object of encouraging closer cooperation among practitioners of human and veterinary medicine and public health officials.

A SUBSTITUTE FOR COUGHING.

METHODS have been evolved whereby a mechanical substitute has been contrived for the act of coughing. It is evident that various pathological conditions may reduce significantly the efficiency of coughing, and serious results may follow. Alvan L. Barach, Gustav J. Beck and William Smith have been working as a team to produce an improved substitute for expiratory flow rates.¹ They have produced several methods by which the retention of pulmonary secretion may be simply overcome by physical methods, which may be employed in poliomyelitis, pulmonary atelectasis, asthma, bronchiectasis and pulmonary emphysema. The first methods exploited were an imitation of the natural process of coughing, using an explosive

decompression, and enclosing the patient in a steel chamber with a baffle device providing a differential chest pressure. The next method tried was that of using the fully inflated lungs with a negative pressure in a respirator. This enabled the elastic recoil of the lungs to empty out a high tidal volume quickly. Other devices combined exsufflation with positive pressure, applied to the chest, or negative pressure applied to the upper respiratory tract. In the present instance the authors describe a method by which a blower is used to inflate the lungs up to 20 to 40 millimetres of mercury positive pressure, together with a negative pressure blower which produces rapid volume flow rates. This contrivance first slowly inflates the lungs, and with the tripping of a valve opens the way for the negative pressure. By this means air is expelled from the lungs at a flow rate greater than that obtained in maximal human coughing. The result achieved is a rapid pressure drop, and time control of the pressure devices may be obtained by a solenoid valve acting on a time-delay relay. Figures are given for the results obtained for normal subjects and for patients with various respiratory conditions. One graph contrasts a maximal cough of 9.8 litres per second in a normal person with a flow rate of 10.8 litres per second produced by the exsufflator. It will be understood that the apparatus inflates the lungs only slowly, so as to avoid driving secretions into the lungs, and enabling the high flow negative phase to extract plugs of secretion. The peak pressure drops below that of the atmosphere in 0.02 second. The authors have found this apparatus of value in cases in which retained bronchial secretions were causing pulmonary atelectasis or impairing the respiratory function. One interesting point is that in experiments on anaesthetized dogs, with 30 millimetres of mercury positive and 40 millimetres of mercury negative pressure, metal objects weighing up to 0.6 gramme previously placed in the lower bronchi through a bronchoscope could be extracted by six to twelve exsufflations with negative pressure.

SYNTHETIC OXYTOCIN.

It is announced in the *Journal of the American Chemical Society* (October 5, 1953) that a group of investigators directed by Vincent du Vigneaud, professor of biochemistry at the Cornell University Medical College, has succeeded in synthesizing the pituitary hormone oxytocin.¹ This is the first pituitary hormone and also the first polypeptide hormone to be synthesized. The molecular weight is approximately 1000. The structural formula shows that the complex molecule contains one representative of leucine, isoleucine, proline, tyrosine, glutamic acid, aspartic acid, glycine and cystine. There are three CONH₂ groups. The presence of cystine confers the characteristic of being a cyclic disulphide. The action of this substance on the uterus is as pronounced as that of the naturally occurring hormone. It is claimed that it has "as high a milk-producing effect as oxytocin"; this probably means as high a milk-expelling effect. One milligramme injected intravenously produced ejection of milk in twenty to thirty seconds. The purified hormone has no action on systemic arterial blood pressure or on excretion of water by the kidney. Vasopressin with pressure and antidiuretic effects is probably similar in structure to oxytocin, but with the leucine and isoleucine replaced by phenylalanine and arginine in beef vasopressin and by phenylalanine and lysine in hog vasopressin.

This successful synthesis starts a new chapter not only in physiology, but in pharmacology and obstetric practice. Often has the charge been laid against endocrine therapeutics that it is the terminal hormone which is employed and not the pituitary agent. To have at hand oxytocin prepared in quantity by the commercial chemist and not laboriously and expensively isolated from the pituitary gland is something which obstetricians must view with pleasure.

¹ *Am. J. M. Sc.*, September, 1953.

¹ A good abstract is given in *Science*, November 6, 1953, page 543.

Abstracts from Medical Literature.

GYNÆCOLOGY AND OBSTETRICS.

Pelvic Connective Tissue.

B. BERGLAS AND I. C. RUBIN (*Surg., Gynec. & Obst.*, September, 1953) suggest that the assumption that the pelvic connective tissue has the function of a supportive structure for the pelvic organs has been based on the supposed presence of band-like condensations of the pelvic connective tissue, their fixation to the pelvic walls and their attachment to the pelvic viscera by sheath-like condensations called visceral fasciae. However, the authors' histological study of sections from female pelvis with intact relationship of vascular and connective tissue components shows the absence of a Mackenrodt ligament and of a pubo-vesico-uterine ligament. The bulk of tissue structures erroneously taken for these ligaments consists of plexuses of blood vessels which are embedded in loose areolar connective tissue. The authors' studies further show that sheath-like condensations of the connective tissue surrounding the pelvic organs, and designated as fasciae, do not exist. None of the microscopic sections show attachment of the pelvic connective tissue to the pelvic walls which could be interpreted as a fixation; moreover, the pelvic connective tissue continues into the retroperitoneal connective tissue of the abdominal cavity. There is no anatomical basis for ascribing support of the pelvic organs to connective tissue structures. The plexuses of blood vessels and the loose areolar connective tissue are inherently incapable of supporting the pelvic organs.

The Fœtal Risk in Breech Presentation.

DOREEN DALEY AND A. M. MICHAEL (*J. Obst. & Gynec. Brit. Emp.*, August, 1953) review a series of 498 cases of breech presentation and discuss the management and hazards associated with such deliveries. Routine antenatal care by the authors includes attempted version, preferably at the thirty-second week of pregnancy. Apart from a careful clinical examination of the pelvis, all *primigravidae* and some *multigravidae* have X-ray pelvimetry if version is unsuccessful. The authors do not favour external version under anaesthesia on account of the satisfactory results achieved by careful vaginal delivery, the risk of failure to turn the baby, the risk of vaginal bleeding and anesthetic risks. Induction of labour by low rupture of the membranes if medical induction fails is performed if post-maturity is thought to be present. The authors stress the advantages of pudendal nerve block anaesthesia, wide episiotomy in the *primigravida* and routine vaginal examination after the membranes rupture for the detection of prolapsed cord. In the 498 cases analysed the patients included 317 *primigravidae* and 181 *multigravidae*, of whom 465 were delivered vaginally and 33 by Caesarean section. There were other significant complications in all but four

of the cases in which Caesarean section was performed. The over-all foetal mortality rate was 13.1%, and no maternal death occurred. The foetal mortality in 231 uncomplicated vaginal deliveries was 2.6%; it rose to 15.9% in complicated cases with babies weighing over five and a half pounds and 28.8% in complicated cases with babies five and a half pounds and under. The authors observed that the foetal mortality was greater with flexed legs (15.2%) than with extended legs (8.5%). Also a high incidence of prolapse of the cord was noticed in this series of breech deliveries (5%). They state that the performance of Caesarean section for all cases with prolapse of the cord early in labour should give improved results. In comparing their results with those of other workers they make a plea for strict criteria of the "complications" of a breech delivery and uniformity in records. They conclude that careful antenatal assessment and vaginal delivery by an experienced obstetrician give satisfactory results in breech deliveries. Elective Caesarean section can be reserved for patients with large babies, associated complications, foetal distress, early prolapse of the cord and uterine inertia.

Ovulation and the So-Called Safe Period.

W. T. POMMERENKE (*J. Obst. & Gynec. Brit. Emp.*, August, 1953) discusses ovulation and its relation to the fertile period and the so-called safe period. He states that since the purpose of ovulation is to consign to the tube an egg for fertilization and the period of viability of the egg is brief (twelve to twenty-four hours), accurate knowledge of the time of ovulation is important in the planning or prevention of a pregnancy. Some women sense the time of ovulation, but by and large ovulation occurs without attracting notice. Moreover, human evolution seems to have dissociated ovulation and sexual desire. Changes in the ovary may sometimes be detected on careful pelvic examination. Routine recording of the basal body temperature affords a simple, fairly reliable means of determining the time of ovulation and planning for pregnancy or its avoidance. Some women are aware of a mucoid discharge which occurs regularly over a one to three day period corresponding with the thermal observations on ovulation. Chemical examination of this mid-menstrual discharge shows the presence of excess carbohydrates of types readily usable by the spermatozoa for metabolism, resulting in a more fluid barrier in the cervical canal. Vaginal smear cytology and endometrial biopsies are routinely used in determining the presumptive time of ovulation. Hormone assays suggest increased production of anterior pituitary hormone at the approximate time of ovulation, a wave of oestrogen elaboration just before and after ovulation and the appearance of pregnandiol in the urine about twenty-four hours after ovulation. The author mentions observations on vitamin C excretion, which, when the vitamin is administered in excess, is said to decrease sharply on the fifteenth day of the cycle. He states that recent work on the changes in electrical potential at the time of ovulation awaits appraisal. A detailed study of 30 pregnancies with known menstrual and coital data is recorded and shows

the date of conception in its relation to the menstrual cycle. Although the majority of conceptions occurred between the twelfth and fifteenth days of the menstrual cycle, with present knowledge the fertile phase cannot be ascertained with exactitude. The author observes that the temptation is to emphasize the rule, not the exception, and that it is to be remembered that pregnancy is a fact, the concept of a safe period is a theory, and the evidence of ovulation is a presumption. He considers that a suitable clinically applicable sign of ovulation is still to be discovered. This would be of vast potential value as a means of pregnancy planning and control.

Diabetes in Pregnancy.

W. S. JONES (*Am. J. Obst. & Gynec.*, August, 1953), in a survey of 184 diabetic pregnancies in a total of 100,962 deliveries, found that 162 reached viability with no hormone therapy. He states that the most important causes of foetal loss are acidosis and toxæmia, which can be combated by good obstetrical care aimed at control of toxæmia and selection of the safest method of delivery, with experienced medical supervision to prevent acidosis, and modern paediatric care of the oedematous and premature infants. Under these conditions, the foetal loss should approximate 10% without the use of hormones, which offer little help in mild and uncomplicated cases of diabetes. The author considers that if hormones are to be used they should be given to the older juveniles, ten-year diabetics and older women. There is no optimal time in weeks for termination of pregnancy and no advantage in routine early delivery at any arbitrary time. Deteriorating control of the diabetes, threatening toxæmia and the appearance of hydramnios are the indications for obstetrical intervention. The indications for Caesarean section should be obstetrical in the broad sense; the necessity for early intervention for acidosis or toxæmia, the increased size of the infants and higher incidence of malpositions will tend to increase the Caesarean section rate, which in the author's clinic approximated 20%.

Primary Malignant Disease of the Female Urethra.

DALE W. RITTER (*West. J. Surg.*, July, 1953) has reviewed the recent literature concerning primary malignant disease of the female urethra and reports an additional 25 cases from the Los Angeles County General Hospital from 1939 to 1951. He states that chronic genitourinary infections and trauma through parturition, coitus, contraception and toilet are thought to be predisposing causes of carcinoma of the urethra. Proliferative lesions of the urethra, such as caruncle, polypus and papilloma, allegedly precede malignant change frequently, and the author considers that these conditions cannot be differentiated from malignant disease by gross examination alone. Of the 25 reported cases the lesion was a squamous-cell carcinoma in 21 cases, an adenocarcinoma in three and a fibrosarcoma in one. Consideration of reported cases indicates that malignant disease of the female urethra commonly occurs in the fifth and sixth decades of life among married and

parous women. The three most common symptoms are unfortunately late manifestations of a disease which has a relatively "silent" onset. These late symptoms are hematuria, dysuria and the presence of a growth. The author describes four pathological groups of urethral malignant disease: exophytic squamous-cell carcinoma, endophytic squamous-cell carcinoma, adenocarcinoma and miscellaneous rare tumours. The exophytic type arises at the meatus, tends to invade the external genitalia and metastasizes to the inguinal nodes. The endophytic type arises in the middle or posterior part of the urethra, tends to invade the bladder earlier and metastasizes to the pelvic nodes. The author stresses the importance of prophylaxis in the form of early treatment of all genito-urinary infections and urethral proliferative lesions. The treatment of reported cases from the literature is tabulated, and the author concludes that the best method of treatment is still controversial. The modern trend of treatment is towards more radical surgery and should, in his opinion, consist of complete surgical extirpation of the primary lesion and a radical bilateral inguinal node dissection in all cases of squamous carcinoma. Radium is used as an adjunct to surgery and in "poor-risk" patients. Details of the 25 reported cases are tabulated and discussed. The author states that the prognosis in malignant disease of the female urethra is poor; he had no five-year cures in the series reported.

The Bleeding in Placenta Prævia.

S. BENDER (*J. Obst. & Gynec. Brit. Emp.*, August, 1953) mentions the difficulties in elucidating the cause of hemorrhage in late pregnancy and reports observations on the causes of bleeding in 112 patients from Mill Road Maternity Hospital, Liverpool. He states that ante-partum hemorrhage with a normally situated placenta may be due to a variety of unrelated conditions, such as toxæmia of pregnancy, trauma following external version or instrumentation, abnormalities of placental development and blood coagulation defects. In 40% to 50% of cases of non-toxic accidental hemorrhage the cause of the bleeding cannot be accurately diagnosed. Although the bleeding from placenta prævia has been considered well understood, there is no reason why all the various causes, known and unknown, of accidental hemorrhage should not also operate with placenta prævia. The author describes three groups of causes of ante-partum bleeding in placenta prævia: (i) "true" placenta prævia due to separation of the placenta consequent on the taking-up of the lower segment (85 cases with a fetal loss of 17); (ii) bleeding due to toxic separation of a placenta prævia (12 cases with two fetal deaths); (iii) bleeding due to other non-toxic causes such as exist with a normally situated placenta (five cases with no fetal deaths). A fourth group is described to include cases in which placenta prævia is diagnosed and treated before bleeding occurs (10 cases and no fetal mortality). No maternal deaths occurred in the 112 cases reviewed, and the total fetal loss (stillbirths and neonatal deaths) was 19 (16.8%). Difficulties were encountered in allocating cases to the four groups described. The chief cause of fetal death in the first group was

prematurity (60%). A review of the second group suggests to the author that toxæmia is not less likely to occur in women with placenta prævia and may be more likely. Some of the patients in this group presented the clinical picture of typical accidental hemorrhage with pain, shock and a tense tender uterus. Others had all the signs of toxæmia of pregnancy with typical painless bleeding of placenta prævia. As a placenta prævia may bleed from toxic separation the author stresses the importance of locating the site of the placenta before treatment is undertaken. Soft tissue radiography (placentography) has been found reliable for the diagnosis of placenta prævia at Mill Road Hospital.

Separation of the Symphysis Pubis.

J. T. CALLAHAN (*Am. J. Obst. & Gynec.*, August, 1953) discusses and reviews cases of separation of the symphysis pubis which have occurred at the New York Lying-In Hospital. The incidence in 65,000 deliveries was 30 cases or one in 2200. The author states that separation may occur either ante partum or at delivery, and the prime symptom is pain in the symphyseal region. Any action causing movement of the symphysis will cause pain—often localized, but sometimes referred to the sacro-iliac joints. The gait becomes "waddling", owing to external rotation of the acetabula and trochanters. There is tenderness over the symphysis—often a palpable defect with tenderness, edema or ecchymosis. X-ray examination may reveal mild to severe displacement. The basic mechanism in production is tractive (external) force, as in a difficult forceps delivery, or expansile (internal) wedge-like force, as in rapid delivery, or long labour with disproportion, causing rupture of the symphyseal ligaments. Forcible abduction of the thighs of a lightly anesthetized patient should be avoided, as it is a common cause of separation. Treatment is generally conservative, with strapping the measure of choice. If surgery is found necessary, wiring is probably the best method. Recovery of function is usually complete, although some separation and movement of the joint may persist. Subsequent vaginal delivery without recurrence of original symptoms can be anticipated.

Pregnancy and Subacute Bacterial Endocarditis.

P. PEDOWITZ and LOUIS M. HELLMAN (*Am. J. Obst. & Gynec.*, August, 1953) review 120 cases of subacute bacterial endocarditis associated with pregnancy; in eight cases pregnancy followed healing of the disease; in 35 the disease was complicated and was cured during pregnancy. The material was collected from questionnaires sent to 300 hospitals, each with 2000 or more deliveries per year. The maternal mortality rate for the series was 6.6%—for the healed groups 3.5% and for the group in which cure took place during pregnancy 14.2%. The authors state that during the first six months after clinical cure, the cardiac reserve is not stabilized, valvular healing is being completed, and the danger of reactivation is still present; pregnancy is therefore contraindicated. In this period there is an increased incidence of con-

gestive failure and an increased maternal mortality rate. Healed subacute bacterial endocarditis of longer duration is *per se* no contraindication to pregnancy, the advisability for which must be determined by a critical evaluation of the underlying cardiac lesion. Pregnancy does not predispose to recurrence of the disease, as the incidence of recurrence during pregnancy is similar to that noted in the healed non-pregnant individual (14.7%). Treatment is as successful in the pregnant as in the non-pregnant woman, and the pre-natal care and conduct of labour are similar to those in any patient with heart disease. The authors recommend the routine intra-partum and post-partum administration of antibiotics to all patients with heart disease to prevent the occurrence or recurrence of subacute bacterial endocarditis.

Accidental Perforation of the Uterus.

W. H. DECKER and B. W. ZANESKI (*Am. J. Obst. & Gynec.*, August, 1953) review the accidental perforations of the uterus which occurred at the Bellevue Hospital between June, 1936, and May, 1952—a period in which first the sulphonamides and later the antibiotics became available for treatment. They state that 10,105 curettages were performed over this period with 51 accidental perforations—an incidence of 0.5%. The indications for operation show that in the group of perforations, 16 patients were curetted for incomplete abortion, 33 for diagnostic curettage and two for hydatidiform mole. No perforations occurred in patients subjected to therapeutic abortion, although this was performed in 170 cases. The sharp curette was the perforating instrument in over half the cases (29), whilst a uterine sound was responsible in most of the remaining cases (18). One death resulted from an unrecognized perforation following the insertion of radium, but there were no other serious injuries or complications. Of the 51 patients affected 27 required laparotomy, and in this group the morbidity rate was considerably higher than amongst those treated conservatively; the authors support the latter method of treatment. They advise laparotomy when the uterus contains infected material or when signs of peritonitis or intraabdominal hemorrhage are present. Intensive antibiotic therapy must be maintained.

The Incompetent Internal Os and Habitual Abortion.

F. E. RUBOVITS, N. R. COOPERMAN and A. F. LASH (*Am. J. Obst. & Gynec.*, August, 1953) present a technique for assessing anatomical lesions of the cervical canal—an aetiological factor in abortions occurring in the second trimester—and discuss the correction of such lesions. By inserting a small rubber balloon into the uterus and filling it with radio-opaque material, the authors can demonstrate by X-ray examination the presence or absence of incompetence of the internal os. Surgical correction of the defect involves excision of a segment of cervix up to and including the cervico-uterine junction. To reduce the diameter of the cervical canal to one-half its size, half of its circumference must be removed.

Special Articles for the Clinician.

(CONTRIBUTED BY REQUEST.)

XCV.

DIAGNOSIS OF LESIONS OF THE STOMACH.

ALTHOUGH one of man's dearest possessions, the stomach is a much abused organ. It bears continual physical and psychic insults, both direct and indirect, and it is little wonder that lengthy maltreatment eventually leads to fractious behaviour or growing resentment. A knowledge of structural and functional anatomy with an understanding of modern biochemistry and physiology is necessary for the surgeon as well as the attending physician. However, in the maze of modern advances, one must remember to understand the individual and his personality pattern as a whole, for at the first turn of the wheel of fate, gastric symptoms are apt to occur. The all-important and time-consuming taking of the patient's history, including habitat, domestic set-up and personal stress factors, must be followed by a careful evaluation of the story obtained, note being made of the site and type of pain, any change in diet or appetite and the exact nature of the dyspepsia. Periodicity and remissions are to be correctly assessed. The clinical examination must be full and complete, including inspection, auscultation and percussion as well as palpation of the abdomen.

The investigations of gastric motility and emptying time, and of intragastric pressure and movements with the aid of barium and radiographic screenings with appropriate posturing by an experienced and careful radiologist, are the most important methods of study of the stomach. Histamine or insulin stimulation of gastric secretion and a fractional test meal estimate of acidity and peptic activity are another. Gastroscopic visualization is also a valuable adjunct in diagnosis in the hands of an expert endoscopist, while one feels that improvement in obtaining adequate material by gastric aspiration for cytological study will prove of benefit in the earlier recognition of disease. At present, unfortunately, difficulties in interpretation of the films preclude its general use. Anacidity is commoner as age advances, so that it has been estimated that 20 out of 100 persons over sixty years of age are histamine-refractory. Anacidity is probably the result of an organic lesion of the gastric mucosa, the atrophy of which is more a stimulus to the formation of carcinoma than is hyperplasia. The incidence of neoplasm is over three times higher in subjects of pernicious anaemia with its associated atrophic gastritis than in the general population. Therefore, such patients should be periodically checked and supervised. There are, of course, limitations to the fractional test meal in the diagnosis of gastric diseases, and wide variations limit the usefulness of the obtained information. Avery Jones states that there is little advantage to be gained from the routine use of test meals in cases of peptic ulceration, but that they may help in the diagnosis of difficult cases with symptoms referable to the upper part of the abdomen in which radiological findings have been negative. Previously there has been a tendency to overlook factors influencing the composition of gastric secretion, including saliva, regurgitated duodenal contents and food residue. The use of insulin and histamine, and the serial test meal technique with dye and the pectin meal rather than gruel, are attempts to obviate psychic response and overcome varied conditions influencing the composition of gastric contents and the interplay between gastric emptying and secretion. Intensive investigations of ulcer and gastritis as cancer precursors and the possible ingestion of carcinogenic substances have failed to produce positive evidence of the causation of gastric carcinoma. The Herman Taylor gastroscope and a competent endoscopist minimize errors, and despite the limitations of blind areas and difficulties in cases in which there is spinal deformity, gastroscopy and fluoroscopic screening together present tremendous diagnostic aids. Gastric biopsy through a flexible gastroscope usually provides specimens from the body of the stomach near the greater curvature, and is of value in studying diffuse lesions in this area, but being blind is of no direct value in studying gastric ulceration or neoplasm. It is most useful in the examination of gastric mucosa in cases of chronic gastritis, whether superficial or atrophic.

Gastric cancer is the cause of one-quarter of the cancer deaths in this country. Ogilvie once cryptically remarked that in relation to carcinoma of the stomach alkalis are the

undertaker's best friend, vividly implying that prolonged use of antacids, without periodic examinations and studies, is poor therapy indeed. Physical examinations may yield entirely negative findings, or may reveal epigastric tenderness and some guarding. The presence of a mass does not necessarily mean a hopeless prognosis, for the bulky polypoid neoplasms are often resectable. Virchow's supraclavicular gland should always be sought for, and a rectal examination is also obligatory. The early diagnosis of cancer of the stomach remains a challenging problem; and despite negative findings from examinations and investigations, a suspicious history and unexplained loss of weight and anaemia suggest that an early laparotomy should be seriously considered. Every gastric ulcer must be considered malignant until proven otherwise, and the only certain method of finding out is by surgical extirpation and histological examination. Therefore, if a gastric ulcer fails to heal and remain healed under correct medical regime in six weeks, an operation is indicated. Certainly, gastric ulcer must in every case be treated to its conclusion, and this is best observed by gastroscopy. In Britain the view is held that the initial lesion is a malignant degeneration with secondary ulceration and that most so-called ulcer cancers are really cancerous ulcers. Other authorities claim that a gastric ulcer carries a 10% chance of malignancy. The size of the ulcer is of no real significance, small lesions often being among the most suspicious. The differential diagnosis may be difficult when the ulcer is situated within the line of the lesser curve. However, the association of a chronic gastric ulcer with achlorhydria sited on or near the greater curvature of the stomach or in the pre-pyloric region with some irregularity of its base or edge is most suspicious of malignant change, particularly if it remains unhealed.

It may be said that gastric ulceration may be produced by anything which causes necrosis of the mucosa of the stomach, thus subjecting it to the digestive action of gastric juice. There are, therefore, many factors in its formation—locally traumatic, vascular, nutritional, allergic, inflammatory, neurogenic and toxic. Clinically, there is an acid peptic factor stimulated by mechanical hormonal and neurogenic causes. Clinical impressions formed from the patient's history and physical examination can be confirmed by radiological, biochemical and gastroscopic examinations. The chronic penetrating ulcer is not difficult to diagnose clinically or radiologically, but X-ray evidence of the acute erosive type may be lacking. The typical crater may be absent also after bed rest and medical treatment have healed the lesion. In many cases after hæmatemesis findings are negative radiologically unless the examination is made in the first few weeks after the bleeding. It is well known that pregnancy, whether the result is due to peace of mind or better dieting, will heal any simple peptic ulcer.

Although there is no obvious cardio-oesophageal muscular sphincter, some extrinsic sphincteric mechanism to prevent oesophageal reflux exists, whether it is due to crural pinch-cock, the sling effect of contracting oblique muscle fibres in the wall of the stomach, a mucosal valvular fold or the angulated infradiaphragmatic oesophageal segment. Laxity of the tissues with deficiency at the oesophageal hiatus is common in later adult life, and herniation of part of the stomach is favoured by conditions raising intraabdominal pressure and by recumbency. Such hernia may be sliding or rolling, and the symptoms are protean. Epigastric discomfort, heartburn and vomiting are common symptoms, varying in intensity according to the degree of reflux. Hæmatemesis and stricture may follow, and this can occur in both the congenital and acquired types in early and late life respectively. The clinical picture of hiatus hernia is sufficiently distinct from peptic ulceration to enable differentiation on history alone, and in cases of doubt, adequate posturing under fluoroscopy, with endoscopy, can provide an accurate diagnosis of this condition.

The relationship between gastric and cardiac disease may be difficult to distinguish, and they may coexist in the aged. Fluoroscopy and the electrocardiogram can help one's clinical acumen in determining the extent of cardiac damage. Substernal pain with gastric ulcer is common, although unrelieved by alkalis and unrelated to effort. Also, of course, a distended stomach causes mechanical and reflex effects on cardiac action. Hæmatemesis is a serious symptom and is commonly due to acute erosions in younger patients or chronic ulcers in the older age group. Although peptic ulcer is the commonest cause of hæmatemesis, the predominant cause of the bleeding must always be sought and, if possible, proved. Bleeding oesophageal varices, carcinoma, hiatus hernia and simple gastric neoplasms, although less common, can usually be diagnosed from a clinical and radiological examination. Experimental and clinical evidence indicates

that portal hypertension with congestion of the gastrointestinal mucous membrane predisposes to peptic ulceration with hæmorrhage from the susceptible congested mucosal tissues or from subepithelial varicosities. Appendiceal dyspepsia is an unsatisfactory diagnosis, and the indiscriminate removal of a "doubtful" appendix in the hope of curing vague epigastric dyspeptic symptoms is to be deplored. The near association of gall-bladder disease must be remembered in the diagnosis of gastric lesions, but the distribution of pain, general clinical picture and, if necessary, result of a Graham's test will differentiate biliary pathological changes.

With cardiospasm there is a narrowing over about an inch of the segment of the oesophagus above the stomach. The sphincteric action is under nervous control, and anomalies of the sympathetic and parasympathetic systems may be causative factors. Barrett states that much confusion concerning the activities of the oesophago-gastric junction would disappear if people distinguished between phenomena of swallowing, which are controlled by muscular movements of the pharynx, gullet and diaphragm, and those of vomiting, regurgitation, belching, rumination and reflux. The latter can occur only if the cardiac sphincter opens, while the former are not influenced by this barrier.

For the future, one hopes that modern techniques will be perfected for the cytological study of gastric aspirate, and that first-class and readily available radiological examinations, combined with gastroscopic studies in specialized units, will assist the clinician to assess his patient's symptoms and signs more speedily. Reliance on a single radiological examination has led to tragic delays in diagnosis and treatment.

ERIC GOULSTON,
Sydney.

British Medical Association News.

SCIENTIFIC.

A MEETING of the New South Wales Branch of the British Medical Association was held on December 10, 1953, at the Robert H. Todd Assembly Hall, British Medical Association House, 135, Macquarie Street, Sydney, Dr. A. J. MURRAY, the President, in the chair.

Chronic Alcoholism.

DR. S. J. MINOGUE read a paper entitled "Alcoholism" (see page 358).

DR. JAMES ISBISTER read a paper entitled "The Effects of Prolonged Alcoholic Excess" (see page 360).

DR. GEORGE HALL said that important points had been brought out. The first was in Dr. Isbister's paper and concerned the relatively high incidence of beriberi heart disease in alcoholism and the observations made about its diagnosis. In England it was regarded as a very uncommon form of heart disease; but it was not uncommon in Australia. Was that because Australians drank more alcohol than the average Englishman? Or were there other factors such as diet or hypersensitivity? The number of occasions on which the diagnosis had been missed in this series was important. If the diagnosis was missed, patients might suffer harm from misdirected treatment or die from lack of specific treatment. One had to remember that in beriberi heart disease one was dealing with heart failure with a high cardiac output and treat it accordingly. It might be dangerous to give mersalyl; he had seen one patient with a wet brain put into *status epilepticus* by it, and it had almost brought about the patient's death. Dr. Hall went on to say that alcoholism could be an important factor in hypertension. Not all chronic alcoholics developed arterial hypertension, but a large proportion did, and it could be prolonged and severe whilst the patient was drinking. He had seen complications of hypertension produced over years, and simply with the withdrawal of alcohol the blood pressure had returned to normal and associated symptoms and signs had resolved.

DR. M. A. O'HALLORAN had two questions to ask Dr. Isbister. The first was whether serum protein estimations were of any value as a check on the patient's dietetic history. He had seen patients who were obviously suffering from malnutrition, yet their serum protein levels appeared to be within normal limits. Dr. Minogue had stated that the adrenal hormones had a relieving effect on the state of stress that was part of the condition. Dr. O'Halloran wondered whether they had ever been tried during the prodromal period of true dipsomania—in that three or four days during which it was

possible to tell that the patient was going on a "bender". Would the giving of ACTH or cortisone prevent it?

DR. S. BENEDEK referred to Dr. Isbister's proportion of 73 out of 86 patients suffering from metabolic illnesses. Dr. Benedek said that at Callan Park they had found that in almost every case of alcoholic psychosis the blood pyruvate level was very much higher than normal. Had it any significance that the pyruvate oxidation system was interfered with?

DR. G. SELBY said that he had been interested in pyruvate metabolism in relation to peripheral neuropathies and had done some work on the subject under the guidance of Professor R. H. S. Thompson at Guy's Hospital, London. Several reports on pyruvate metabolism in alcoholics had appeared in the literature. Taylor and McHenry included alcoholics in their paper on acute thiamine deficiency published in *The Canadian Medical Association Journal* in November, 1949, and Worts, Bueding, Stein and Jolliffe had described pyruvic acid studies in the Wernicke syndrome in *Archives of Neurology and Psychiatry* of February, 1942. There appeared to be no doubt that alcohol had no direct toxic effect on the pyruvate oxidase system, and that the failure of the complete metabolism of pyruvic acid was simply due to thiamine deficiency and the result of the chronic alcoholic's neglected diet.

PROFESSOR W. S. DAWSON said that he had one or two questions to ask Dr. Minogue. In the first place, he thought that Dr. Isbister's observation of weakness in the beriberi cardiac syndrome appeared to be correlated with Dr. Minogue's observation of a complaint of fatigue in his patients. Incidentally, he (Professor Dawson) wished to ask Dr. Minogue whether a feeling of excessive tension was not at least as common as a feeling of fatigue as one of the alcoholic's outstanding symptoms. Referring to the commission of crimes during a state of alcoholism, Professor Dawson wondered whether alcohol was not taken to give so-called "Dutch courage" by people who were proposing or wishing to commit some crime, so that they felt the need to reduce their inhibitions by imbibing alcohol. Referring to Dr. Minogue's views on the relationship between dipsomania and manic-depressive psychosis, Professor Dawson said that dipsomaniacs seemed to pass through an unhappy, depressing stage before they resorted to alcoholism as an escape. Dr. Minogue had also mentioned the dry texture of the skin of alcoholics; Professor Dawson thought that it might be ascribed to the "pickling" process which the internal organs seemed to undergo. Professor Dawson asked both Dr. Minogue and Dr. Isbister whether they had any information as to the mortality statistics in Australia, especially in view of the considerable increase in the consumption of alcohol during the last ten or fifteen years. In England, apparently, the number of deaths ascribed to chronic alcoholism and to cirrhosis of the liver had been steadily dropping in recent years, over a period when the consumption of alcohol per head had also declined. What was the position in Australia?

DR. N. E. B. KIRKWOOD said that he had been for two years at the Reception House, Newcastle, and was handling acute and chronic alcoholics all the time. There they were able to keep them for a time and he had become interested in their treatment. Dr. Kirkwood said that he had attended meetings of Alcoholics Anonymous, not, as Dr. Minogue, from the inside looking out; he had been struck by what was characteristic of a great number of alcoholics, their exhibitionism—they were narcissistic, homosexual, or something between the two. Dr. Kirkwood said that he was of the opinion that heterosexual development was not so common in the inebriate as in the general population. That perhaps accounted for the large number of single people among alcoholics. In women, inhibitions were gone. When one saw members of Alcoholics Anonymous talking, one got the impression that they thought themselves the most important people in the community. The depressive was another type of person who tended to become an inebriate. A bout of alcoholism was often preceded by a bout of depression. With reference to the presence of homosexuality, Dr. Kirkwood said that he had found on checking the public hair distribution that many male alcoholics had the female triangle. Referring to the use of insulin in the treatment of alcoholism, Dr. Kirkwood said that at Newcastle he had given none at all for twelve months or more. It used to be the custom to give liver extract if the alcoholic patient was anæmic; now every inebriate received liver extract, and insulin seemed unnecessary. Dr. Kirkwood wondered whether the liver was the key gland. All patients were given daily injections of the B group vitamins, and they appeared to pick up. He had been interested in Dr. Isbister's series of cases, in which there was no nephritis or uræmia. He used to think that alcohol was one of the great causes of nephritis. Certainly one person had been admitted to the

Reception House dying of uræmia, and the post-mortem examination revealed that nephritis was one of the causes of death. Reference had been made to hæmatemesis, but he had heard no reference to melæna. Only a few weeks previously a young man had arrived in an ambulance at the Reception House with acute melæna; he was sent to the Royal Newcastle Hospital and died in a few hours. Melæna as well as hæmatemesis was one of the conditions resulting from excessive alcoholism.

Dr. E. J. A. NUFFIELD said that the speakers had shown up the prevailing abysmal ignorance of the subject. He disagreed with Dr. Minogue's statement that the problem was purely medical. There were social aspects of alcoholism which perhaps transcended their capacities or capabilities. There were two problems in ætiology: the biological problem (why was there idiosyncrasy to alcohol?) and the sociological problem, which concerned the pattern of drinking in different communities. The community recognized that the problem was not only that of the medical profession, but also had social and legal implications. Dr. Nuffield said that, working in a general hospital as he did, he was struck by the frustration in treating the epiphenomena of alcoholism. Why had one person an idiosyncrasy to alcohol? And what determined the social pattern of drinking? In the elucidation of the former problem work was needed by the medical profession and its members should take note of what their legal friends were doing in relation to the sociological problem. It was known that different races had different incidences of alcoholism. Perhaps it was in the field of genetic research that the reason for this could be elucidated.

Dr. DOUGLAS ANDERSON said that one or two practical points had not been expressed. There was a class of hard drinker who found his way to the doctor, not to the Reception House or a general hospital, and who very badly wanted help, but who was unlikely to give up drinking. As Dr. Minogue had said, alcoholics must not be moralized at or sermonized at. If the doctor did that, it would induce the patient at the next visit to conceal how much he had taken. Much more cooperation would be obtained if the doctor gave advice on the following lines: "A great deal can be done for you to improve your condition during your interval of abstinence. Let us get busy and see what can be done." Dr. Anderson said that he was impressed by the result of a draught of kaolin stirred up in a large glass of water and taken each morning and evening. It had a good effect on chronic gastritis. He had also had good results from the administration of methionine to the person who had been drinking heavily; five grammes was not too much for a first dose, then five grammes were given every day for a few days. In addition, any recognizable vitamin lack could be corrected. There was another class of alcoholic patient who went to the doctor, whose drinking was a manifestation of gluttony. The doctor's main point of contact was the liver, which could often be felt; a good effect could be obtained by showing him the red colour which resulted when Ehrlich's aldehyde reagent was added to the urine. The best thing to do was to gain as much of the patient's cooperation as one thought one could get and to demonstrate the improvement that would take place in the state of his liver during a brief period of abstinence. Dr. Anderson said that it seemed to him that there was much more to be achieved by promoting the patient's general health and domestic well-being than by taking a severe line.

Dr. W. E. FISHER said that one speaker had paid tribute to Dr. Minogue's separation between the hard drinker and the dipsomaniac. If he had any criticism of Dr. Isbister, it would be for having grouped the varieties of cardiac beriberi too closely together. Dr. Fisher thought it important to remember the text-book classification of acute cardiac beriberi. It was a very real clinical entity of sudden onset and grave import (death would occur within twenty-four to forty-eight hours if nothing was done), and provided one of the most spectacular responses to treatment in medicine if thiamine was given; five or ten milligrammes were enough to bring the apex beat in from the axilla to the mid-line and dissipate the so-called death rattle. Dr. Fisher said he thought it most important to keep that form of heart disease apart from other disorders of the heart; if something was not done quickly the patient would die. The other cardiac manifestations attributed to beriberi he regarded with more circumspection. He did not question the diagnosis in Dr. Isbister's group, but there were other causes of œdema, such as malnutrition; there were other causes of fatigability and debility; and there were other causes producing evidence of impaired myocardial reserve; the finding of any or any group of these manifestations, even against a background of alcoholism in the history, did not necessarily mean that the patient was suffering from beriberi heart, particularly if the knee jerks were still present. Dr. Fisher said that he spoke with some knowledge in the matter. He had had the experience of some 90 patients diagnosed as suffering from cardiac

beriberi; he had dissented from the diagnosis, taken them away from the medical officers in charge and put them in charge of others, and given them graduated physical exercise. In six weeks' time, instead of dying, they all went out of hospital and undertook strenuous work.

Dr. Minogue, in reply, referred first to the question of the single man and his bad diet and said that the figures given by Dr. Isbister, in his opinion, were too high. He himself had found that married men predominated amongst chronic alcoholics. The single man showed the effect of chronic alcoholism faster, perhaps because of his poor diet. Women were content to be "wardrobe drinkers"; they did not have to face the cares of the world. Dr. O'Halloran had asked whether it would be possible to cut short an attack by giving injections before it. Dr. Minogue said that he had had no experience, but he did not think one could get hold of such a patient. During the stage before a bout of drinking alcoholics were very arrogant and "up in the air", and if such a suggestion was made it would be received with hostility. In reply to Dr. Benedek, Dr. Minogue said that mostly alcoholics were not tense; they were tired mentally and physically. He thought that what had been said about the removal of inhibitions was probably quite correct. He had never been able to establish any relationship between dipsomania and manic-depressive insanity. In the dipsomaniac there were definite mental and physical characteristics which were entirely missing from the manic depressive. Sudden deaths did occur in *delirium tremens*. The patients were very florid and very restless, and convulsions had occurred. Dr. Minogue thought that death was due to coronary occlusion. In certain cases the cause was unknown. Dr. Minogue said that Dr. Kirkwood's question was interesting, but Reception House practice was very different from private practice; the former type of patients were much more acutely alcoholic and violent. Dr. Kirkwood had accused the members of Alcoholics Anonymous of being exhibitionists. It was a strange thing that alcoholism was most prevalent amongst the Scottish and Irish. In New York, for every Jew affected, 40 Irishmen became dipsomaniacs. Dr. Kirkwood had referred to glandular dystrophy, female hair distribution and homosexual trends; Dr. Minogue said that no greater insult could be offered to the Scottish and Irish. It was also a fact that some of the ablest men in letters had been dipsomaniacs—Henry Lawson, Christopher Brennan, Robert Burns and Christopher Marlowe amongst them. The point of view of employers was that those of their employees who became dipsomaniacs were the best workmen and the most intelligent. Probably they had some glandular dystrophy; but that did not make them homosexual. The dipsomaniac had only one habit, and that was drinking; he had no time for or interest in other vices. Dr. Minogue went on to say that when he had started Alcoholics Anonymous in Sydney ten years earlier opposition had been very bitter, and it still persisted. The members of the medical profession would not accept anything novel or anything new; possibly in this instance it was because of the spiritual aspect involved. Dr. Minogue said that if any of those present had any doubts about the type of people in Alcoholics Anonymous, particularly Dr. Kirkwood, he would be interested to arrange a debate between its members and any university people chosen. The antagonism displayed had certainly surprised him. The question of the drinking habits of nations had nothing to do with the problem. Ten years earlier Australians had had the idea that they were different from other countries; the plain fact was that they were exactly the same. It did not matter who alcoholics were or what their nationality, they still had the same compulsion to drink. No one knew why the Jews seemed immune to alcoholism. Dr. Minogue did not know whether there was a genetic factor in alcoholism. He saw many hard drinkers. All that was necessary was to point out to them that it had become a problem and that the most logical thing was to give it up; if the patient could be made to see the position logically he would probably give up drinking. If the patient could be induced to cooperate things could be done with him; if not, nothing could be done.

Dr. Isbister, in reply to Dr. Hall, who had referred to the incorrect treatment of beriberi heart disease, said that he had seen two patients with beriberi develop anuria after mersalyl had been given. The serum protein estimation was a very poor indication of malnutrition; if a low serum albumin level was found it was more likely to be an indication of liver disease. Dr. Isbister said that he had no information on the mortality from chronic alcoholism; his own figures did not mean a great deal, but they probably meant a little more than the Registrar-General's figures. On the subject of uræmia, Dr. Isbister said that he looked on the term as a cloak of ignorance. When anything "went wrong" with a medical or surgical patient he was at once said to be suffering from uræmia. Very few of the patients under discussion had renal failure. Many were admitted to

hospital with so-called uræmia, but they were suffering from many other things. Dr. Anderson had mentioned methionine; Dr. Isbister said that he thought it rather an expensive means of giving essential amino acids; why not give the patients milk and eggs? In reply to Dr. Fisher's remarks on beriberi heart disease, Dr. Isbister said that there were other causes of oedema, but the patients in his series all had increased venous pressure and evidence of cardiac failure. He believed that cardiac beriberi of some degree or other was present, but some patients in the later age group might have been affected by some other contributing factor.

Dr. Murray, from the chair, said that the papers had covered much original work, and the discussion had been the most interesting he could remember at such a meeting. Alcoholism had developed from a social habit to a social evil, and the members of the medical profession should take stock of the position. Dr. Murray said that he had not been aware of the hostility to Alcoholics Anonymous; he was sure that all those present were glad that Dr. Minogue had had an opportunity to set out his case "from within". Dr. Murray was impressed with the work of Dr. Minogue and knew that he had tackled the problem at an earlier stage than the rest of those present did. He thanked both speakers, and also those who had taken part in the discussion, for an instructive and entertaining meeting.

Medical Societies.

MEDICAL SCIENCES CLUB OF SOUTH AUSTRALIA.

A MEETING of the Medical Sciences Club of South Australia was held in the Anatomy Theatre, New Medical School, Frome Road, Adelaide, on November 6, 1953.

Surgery of the Heart and Great Vessels.

DR. H. D'ARCY SUTHERLAND presented an outline of the history of the development of surgery of the heart and great vessels and described the common congenital and acquired lesions, together with the physiological disturbances in the circulation. He also considered the main clinical features and the methods by which the abnormal blood flow and blood gas estimations were used in diagnosis and estimation of the degree of disability. He gave an account in some detail of the technique of cardiac catheterization by angiocardiography, as well as an outline of the surgical treatment of patent ductus arteriosus, tetralogy of Fallot, coarctation of the aorta and mitral stenosis, with a series of slides demonstrating many of the steps at operation. Some of the work being done in cardiac centres overseas on mitral regurgitation, atrio-septal defect, transposition of the veins, heart-lung preparations and modern cooling techniques was discussed as an indication of the development which could be expected in this very progressive field of surgery.

Epidemiology of Sheep Parasites.

MR. A. W. BANKS discussed the epidemiology of sheep parasites. He said that the following was a summary of the typical life history of sheep intestinal parasites: adult females and females in intestine—eggs pass out in host's faeces; stage 1 larvæ; stage 2 larvæ; stage 3 (infective) larvæ—ingested by host; stage 4 larvæ—adult worms. Egg output was enormous, each adult female worm producing several hundred to 10,000 eggs per day. As many as 20,000 worms were commonly present, and each sheep might be distributing five to thirty million eggs per day. Parasitologists aimed to exploit vulnerable phases of the cycle to tip the balance in favour of the sheep, economically and without disruption of farming practices.

Eradication of worms was impracticable, at least at present. The following were controlling factors at various stages: (i) Hatching of eggs: oxygen, warmth, moisture. (ii) Stage 1 and 2 larvæ: oxygen, warmth, moisture plus bacteria *et cetera* for food; man's intervention then added little to the great mortality due to climatic factors. (iii) Stage 3 (infective) larvæ on the ground: oxygen, warmth, moisture; time; access to sheep. Those larvæ did not feed, but depended on stored energy; when that was exhausted they died. Access to sheep required a film of moisture to assist larvæ to move up grass blades, and diffused light, but if the host was not at hand, larvæ soon exhausted themselves. (iv) Stage 3, larvæ in the host, and stage 4 larvæ. Allergy and active immunity protected the

host more strongly after successive experiences. With warm genera common in South Australia, that immunity usually became permanent and solid. It was not fantastic to visualize young sheep deliberately dosed with larvæ instead of anthelmintics. (v) Adult worms. Those might be expelled by drugs with varying degrees of efficiency, but the parasitologist liked to regard such treatment as an index of failure of control. It was economic salvage.

Adult sheep were the source of both infection and immunity for young sheep. The balance might be regulated to a considerable degree by appropriate animal husbandry. Studies in progress aimed to uncover the local epidemiological pattern. It seemed that the low humidity of South Australian summers protected the wool industry from widespread parasitism, and that considerable savings could be made in present expenditure on anthelmintics.

Electron Micrography of the Pancreas.

PROFESSOR J. S. ROBERTSON briefly discussed techniques which had led to the introduction of efficient methods whereby sections could be cut thin enough (not more than 0.1µ) to be examined in the electron microscope. He said that all the important advances in those methods had been made in the United States. The earlier attempts had involved the use of a knife which rotated very rapidly and cut through the tissue at almost sonic speed. That, however, had proved too difficult for routine use. It later proved possible to cut very thin sections with a conventional microtome with either a mechanical or thermal advancement. At that stage, the problem of fixation began to be seriously attacked, and at present the best fixative devised appeared to be 1% osmic acid solution buffered to pH 7.4 with an acetate-veronal buffer (Palade, 1952). The introduction of methacrylate embedding was also a great advance, as was that of the glass knife.

The paper was illustrated by electron micrographs of the normal mouse pancreas fixed in buffered osmic acid and cut in methacrylate with a glass knife on a geared-down rotary microtome. A feature of the micrographs was the presence of very numerous cytoplasmic double membranes in the acinar cells. In many cells, separation and vacuolation of the membranes could be seen. Among other features revealed by the electron microscope were small finger-like projections on the free borders of the duct epithelium and on the free (ductal) border of the acinar cells. Islet granules were small, circular and very dense. Mitochondria were conspicuous in both acinar and islet cells, and showed the characteristic complex internal ridges seen in these organelles in very many other animals and tissues.

Out of the Past.

In this column will be published from time to time extracts, taken from medical journals, newspapers, official and historical records, diaries and so on, dealing with events connected with the early medical history of Australia.

VELOCIPEDES AND RUPTURES.¹

[The Australian Medical Journal, June, 1869.]

A CORRESPONDENT of one of the daily papers, referring to a statement made in the *Daylesford Mercury* that the reason why velocipedes went out of fashion nearly forty years ago was because the exertion required in driving them had a tendency to produce ruptures, says: Referring to the above, I should wish to prevent any anxiety which might be occasioned on reading it. Forty years ago there was no such velocipede in existence as the latest French and American ones. The nearest approach to them were what were called the "dandy horses" with only two wheels, one in front of the other, but instead of being worked with cranks, were propelled by the feet touching the ground: the exertion of doing so—some machines being higher from the ground than others—caused ruptures or had that tendency, hence they were discarded. Those now in use work with cranks made to suit any length of leg so that there can be no such danger as alluded to any more than walking.

¹ From the original in the Mitchell Library, Sydney.

Correspondence.

CORNEAL ULCER.

SIR: I would like to thank Dr. D'Ombain, of Sydney, for his courteous reply to my letter concerning his essay on corneal ulcer. However, I still think his advocacy of vigorous application of atropine to be highly dangerous in elderly patients, and I hope general practitioners will not follow his advice, or disaster will follow.

Yours, etc.,

F. W. SIMPSON, D.O. (Oxon.).

105 St. George's Terrace,
Perth,
February 5, 1954.

SIR: Arthur D'Ombain, in his letter (January 23, 1954) replying to my criticism of his article on corneal ulcer, agrees that he may, at certain points, have written above his readers. He suggests that I, personally, am incapable of applying an adhesive strip. This may well be so, but it is quite beside the point. I criticize his article because he recommended the use of cortisone, carbolic, atropine *ad libitum* and adhesive strips after cocaine by men whose eye work forms only a small part of their practice. I say this is dangerous, and it is dangerous whether or not I know how to apply an adhesive strip. He says the article concerned corneal ulcer, not iritis; was it not for the iritic complication of ulcer that he recommended atropine? I appreciate his kindness in hoping that I never get a corneal abrasion, but that if I do I consult a man who is quick on the trigger with the atropine. If I get a corneal abrasion and if the man I consult slops atropine into my eye without further ado, then there will be one less ophthalmologist in Brisbane. Justifiable homicide. No jury would convict.

Yours, etc.,

JAMES HART.

137 Wickham Terrace,
Brisbane,
February 11, 1954.

COMPARISON OF DIFFERENT TYPES OF X-RAY FILMS FOR CASE FINDING AND DIAGNOSIS OF SILICOSIS.

SIR: In the journal of February 6, 1954, there appears a contribution entitled "Comparison of Different Types of X-Ray Films for Case Finding and Diagnosis of Silicosis".

I lost interest in this paper when I read that the observers were ignorant of the medical and occupational histories of the subjects. This reduced the investigation to a guessing competition.

Radiology cannot be divorced from the other clinical methods of examination. Even the most elementary textbooks insist on the correlation of the clinical and radiological findings and state that even better results are obtained where the physician and radiologist meet in consultation.

I would be very loath to give an opinion on a chest film without knowing the age and medical history of the patient.

At the meetings of the Medical Authority of the Silicosis Committee in New South Wales, three physicians and a radiologist consider a complete medical history and the X-ray films before coming to any conclusions.

Yours, etc.,

J. G. EDWARDS.

185 Macquarie Street,
Sydney,
February 9, 1954.

DIFFUSE CARCINOMA OF THE BREAST.

SIR: Mr. Yeates has quoted four authorities alleged to support radical mastectomy for patients such as his. On accepting his invitation to consider these quotations "calmly", I find that they do not support his position.

1. Adair, discussing the contraindications of Haagensen and Stout, states that he would operate in some cases of

pregnancy and lactation, but he says nothing about diffuse inflammatory carcinoma, which has been shown by Mr. Yeates's authorities to be quite distinct from carcinoma in pregnancy and lactation. (Mr. Yeates's patient may be quoted as an example of this distinction, for she was neither pregnant nor lactating.) Moreover, Haagensen and Stout state that widespread *peau d'orange* is a contraindication to operation, and Adair takes no exception to this.

2. T. G. Orr refers to the unpredictable tendency of carcinoma to remain localized or to metastasize early, requiring a flexibility of rules and a seasoned judgement, and he advocates operation when "no extension of the tumor is found beyond the area which may be removed by the radical operation". But, with diffuse gross enlargement of the breast, involvement of axillary glands and widespread oedema of the skin over the breast, as in Mr. Yeates's patient, the opportunity of flexible rules, seasoned judgement and radical operation has long passed. There is no longer a question whether the growth remains localized or has metastasized early. There has already occurred a lymphatic blockage by centrifugal spread of carcinoma, not to one point of the periphery, but to all points, including the supra-clavicular, internal mammary and opposite side, not a minor lymphatic blockage, but a blockage which is widespread and circumferentially almost complete, involving not only the usual anatomical pathways, but also the alternative pathways. Orr particularly urges young surgeons to observe the contraindications laid down by Haagensen and Stout, including widespread *peau d'orange*. He quotes Celsus: "There is not so great a danger of cancer, unless it be irritated by the imprudence of the physician."

3. Meyer, Dockerty and Harrington, the Mayo Clinic surgeons, similarly exclude from operation those patients in whom the disease had "obviously spread beyond the limits of excision", and they likewise give no sanction for operation in the presence of widespread oedema of the skin over the breast. Even in the group selected for operation, the less extensive cases, the results were not encouraging, three patients out of 63 surviving for five years. One survived for five years without operation.

4. The position in regard to Marshall and Hare (the Lahey Clinic surgeons) is peculiar. They aimed to standardize treatment, and selected radical mastectomy with post-operative radiotherapy as their standard method. They excluded a series of patients from this standard treatment and treated these by other methods, such as radiotherapy, simple mastectomy *et cetera*. Presumably these were more advanced cases, like Mr. Yeates's patient. In their article they exclude this section from study and refer from then onwards only to the selected series in which no further attempt at grouping or selection was made, and to which standard treatment was applied. They make no reference to acute inflammatory carcinoma, which we are discussing, nor to widespread *peau d'orange*, so their advice is irrelevant to this discussion. But Mr. Yeates lifts only one corner of the curtain and that only slightly. His quotation appears to refer to all the Lahey Clinic cases. His readers could not recognize that it refers only to one group, the group which is unlikely to contain patients such as Mr. Yeates's. His readers would not even suspect the existence of separate groups. Mr. Yeates has omitted the opening clause, "In this series", from his quotation, and has begun his quotation with a capital "W", not in the original.

5. Mr. Yeates states that, "Even in the failed cases no very great harm has been done. *Life may be shortened for a few months*". (The italics are mine.) Herein he reveals to me the fundamental difference between our points of view.

Over and above the general misery and disability inseparable from a major operation, there is something particularly harmful in the radical mastectomy for patients with widespread *peau d'orange*. Sir Stanford Cade (1948) writes of this: "I wish to emphasise the incalculable harm done by radical mastectomy . . . the operation does not prolong life; it seems, in some cases, to open wide every channel for the uncontrollable spread of the disease."

6. "On the credit side there is the satisfaction to all concerned that the patient has been afforded the best known chance of survival." Mr. Yeates here takes for granted that which he set out to prove.

7. "Although a patient may fear an operation for cancer she is much more fearful if abandoned." This is irrelevant. The choice is not between operation and abandonment.

8. "Doses of radiotherapy are not likely to have any effect on a heavy diffuse breast." How then do they affect the *cervix uteri*, oesophagus and mediastinal glands, which are even more deeply situated than tissue in a heavy breast?

9. "Ulceration, infection and foul discharge" are given as reasons for the radical operation. But there is little tendency to these in patients with diffuse inflammatory carcinoma treated conservatively. If they occur, they may be treated by simple mastectomy.

10. "The trend of today is to extend the scope of surgery." This is a half-truth. There is a second trend, and that is to more conservative surgery. It is the more striking trend, and it is led by McWhirter in Edinburgh, the Saint Bartholomew's School in London, and by biochemists and endocrinologists.

11. "The five-year survival rate has recently shown the first significant increase since Halsted." That is wrong. The survival rates reported by Gordon-Taylor and many other surgeons improved significantly on Halsted's. The statement is also irrelevant. Improvements in survival rates since Halsted, recent or not, have not been due to the treatment of diffuse inflammatory carcinoma of the breast by the methods advocated by Mr. Yeates.

12. Finally, there remains the most remarkable feature of Mr. Yeates's case report—the advocacy of a therapeutic procedure on the basis of one case, and that a failure.

Yours, etc.,

V. J. KINSELLA.

235 Macquarie Street,
Sydney,
February 13, 1954.

Reference.

CADE, STANFORD (1948). "The Treatment of Cancer of the Breast", *Proc. Roy. Soc. Med.*, 41: 129.

REGURGITATION AND VOMITING DURING INDUCTION OF ANÆSTHESIA.

SIR: I would like to support Dr. Brand's criticism of Dr. Wolfers's method of induction, and at the same time submit a few comments on statements made in his letter.

It is my contention that there is little likelihood of regurgitation if the table is tipped into a reverse Trendelenburg position (10° to 15°) until intubation is effected and the cuff inflated. It is my practice to perform this with succinyl choline chloride preceded by minimal thiopentone. The degree of tilt mentioned does not seem to have any appreciable disturbing effect on the cardio-vascular system, as would the sitting posture mentioned by Dr. Wolfers.

In further criticism of Dr. Brand's method I cannot see how he could intubate "at leisure" an apnoeic patient through a pool of regurgitated fluid. An undesirable degree of anoxia would soon be evident, and any attempt to obviate this by inflation of the lungs with oxygen before intubation could result in the fluid being forced into the respiratory tract, with further aggravation of the anoxia.

I feel there is one other point in Dr. Brand's letter which demands comment—that is, his use of a full dose of thiopentone. It is well known that this agent will often cause a considerable fall in blood pressure, which in the "poor risk" case may prove fatal. A minimal or "sleep dose" of this drug is quite sufficient and immeasurably safer.

Yours, etc.,

7 Malcolm Street,
Perth,
February 8, 1954.

L. G. B. CUMPTON.

RECENT EXPERIENCES IN THORACIC SURGERY IN NEW SOUTH WALES.

SIR: Mr. Douglas Miller (January 23, 1954) has hit the nail on the head with customary precision when he describes as "contemptuous sessional pittances" the emoluments of many of those toiling in such specialized fields as neurosurgery and thoracic surgery.

The system of sessional payments in general, as opposed to salaries computed on a sessional basis, has little to recommend it apart from the assistance it may give to specialists establishing themselves in practice. The two glaring anomalies in this regard are, firstly, that payment is greater for the slower than the faster and presumably more efficient surgeon, and secondly, that if for any reason—an unexpected pyrexia on the part of the patient, the sudden indisposition

of the anaesthetist, or even the blocking of the theatre drains—no work can be done, the surgeon suffers financially without the slightest hope of recompense. This applies particularly to thoracic surgeons, much of whose income is derived from work of this kind.

The anaesthetist, too, must set aside similar sessions. This may be a morning or even a whole day, and as it is but rarely that the absence of work is announced until late on the afternoon before, the likelihood of alternative employment is extremely small. This is a matter of grave concern to those, highly qualified technically, who work with thoracic surgeons and neurosurgeons. There is no place in these spheres for the "occasional anaesthetist". He or she must be an integral and regular member of the team, who understands the needs and problems of the surgeon as well as those of the patient.

At present, a surgeon working at the Repatriation Hospital, Concord, or the Thoracic Unit of the Royal North Shore Hospital, is paid about £5 for the removal of the whole or part of a lung, and his anaesthetist is similarly rewarded. The former would be better off financially by seeing two new patients in his rooms, a procedure most unlikely to take more than an hour, and probably much less. The latter would get £5 5s. for an anaesthetic on an injured worker suffering, for example, from an inguinal hernia, if the operation lasted between thirty minutes and one hour, the fee in this case being paid by one of the insurance companies, none of whom are commonly regarded as philanthropists.

Senior members of the profession in this city, to whom the young might reasonably expect to turn for help, advice and leadership, usually give the impression that they think talk of money in this fashion is either a deplorable lapse of taste, flirting with the boggy of nationalized medicine, or both. Surely, however, we have arrived at a stage when facts must be faced. This work is concerned largely with the under-privileged, many of whom suffer from tuberculosis, and whose treatment must be regarded as a state or national responsibility. Thoracic surgeons, therefore, and the anaesthetists who work with them, must look to these authorities for adequate remuneration.

At the Alfred and Repatriation Hospitals in Melbourne, to mention but two, salaries computed on a sessional basis have been for years an accepted means of dealing with some of the problems of these two specialties. The payment of anaesthetists, particularly for morning sessions, is also a well-established practice in general hospitals in that city, so the suggestions mentioned above can hardly be regarded as revolutionary and therefore suspect.

Until the introduction of some arrangement to permit skilled anaesthetists and thoracic surgeons to reserve fixed times for operating sessions without fear of financial hardship, there can be little incentive for young graduates to undertake this work, whose continuance—at a high level of proficiency—must play so important a part in the eradication of pulmonary tuberculosis in this country.

Yours, etc.,

143 Macquarie Street,
Sydney,
February 15, 1954.

J. F. McCULLOCH.

TRAINING FOR GENERAL PRACTICE.

SIR: Attention is drawn to an announcement in the journal, by the Post-Graduate Committee in Medicine of the University of Sydney, of a series of conferences on graduate and post-graduate medical education, which will be opened by the Chancellor of the University, Sir Charles Bickerton Blackburn, at the University on the evening of Monday, May 3, 1954.

The subject for discussion on this evening will be "Training for General Practice", and the date has been arranged so that it will fall during the general revision course in order to give an added opportunity for country general practitioners to attend.

The first conference will take the form of a panel discussion, on which the University, the Post-Graduate Committee, the British Medical Association, general practitioners and others will be represented. After the matter has been introduced by the panel, it will be open for general discussion and for recommendations to be made to the committee. The dates for discussion of the other subjects—"The Training of the Specialist" and "The Post-Graduate Training of the Practising Doctor"—have not yet been fixed, but will be announced later.

In arranging for "Training for General Practice" to be the subject of the first conference, the committee hope for a discussion of our present methods of training in New South Wales, especially in the light of the recent trends in medical education. In the words of the Report of the Committee on General Practice and the Training of the General Practitioner of the British Medical Association (1950), general practice must be regarded as "a special form of practice, which must be founded on general basic principles and appropriate postgraduate study" and which requires its own special training.

Many universities and hospitals overseas have introduced teaching and training general practices, trainee assistantships in general practice, general practice residencies and general practice programmes for resident medical officers. Already some residencies and programmes of this type and of high standard have been introduced in New South Wales.

The committee have also completed a review of hospitals in New South Wales from the aspect of their potential in the training of specialists and general practitioners. This will shortly be printed, and copies will be available on application.

The committee is of the opinion that these matters are of considerable importance in the development of graduate and post-graduate medical education in New South Wales and is anxious that the conference should be brought to the notice of as many of the bodies concerned and persons interested as possible. They would also appreciate any comments or suggestions concerning these matters.

Yours, etc.,

V. M. COPPLESON,
Honorary Director, The Post-Graduate
Committee in Medicine in the University of Sydney.

131 Macquarie Street,
Sydney,
February 17, 1954.

Post-Graduate Work.

THE POST-GRADUATE COMMITTEE IN MEDICINE IN THE UNIVERSITY OF SYDNEY.

Conferences on Graduate and Post-Graduate Medical Education.

THE Post-Graduate Committee in Medicine in the University of Sydney announces that it proposes to hold the following conferences on graduate and post-graduate medical education: (i) "Training for General Practice", (ii) "The Training of Specialists", (iii) "The Post-Graduate Education of the Practising Doctor".

The first of these conferences, "Training for General Practice", will be held at the School of Public Health and tropical medicine at 8 p.m. on Monday, May 3, 1954, during the annual revision course, and will be opened by Sir Charles Bickerton Blackburn, Chancellor of the University. Details of the second and third conferences will be announced later.

Attendance will be by invitation, and all bodies wishing to be represented, or persons wishing to attend the first or subsequent conference, should communicate as soon as possible with the Post-Graduate Committee in Medicine, University of Sydney, 131 Macquarie Street, Sydney (BW 7483).

General Revision Course.

The Post-Graduate Committee in Medicine in the University of Sydney announces that the annual general revision course will be held for two weeks from Tuesday, April 27, to Friday, May 7, 1954, inclusive, under the supervision of Dr. J. W. Graham. The programme is as follows:

Tuesday, April 27: 9 a.m., registration; 9.30 a.m., opening of course by the Vice-Chancellor of the University of Sydney, Professor S. H. Roberts; 9.45 a.m., election of chairman; 10 a.m., review of course; 10.45 a.m., seminar on gastroenterology, "Affections of the Oesophagus", Dr. F. W. Niesche and Dr. S. Goulston; 11.45 a.m., "Persistent Vomiting in the First Year of Life", Dr. Kathleen Winning, Dr. T. Y. Nelson and Dr. George Sylvester; 2.15 p.m., "Infestations of the Alimentary Tract", Dr. George Hall; 2.45 p.m., "Anemias in Relation to the Alimentary Tract", Dr. Edgar Thomson and Dr. C. R. Bickerton Blackburn (to be confirmed); 3.45 p.m., film, "Complications of Peptic Ulcer".

Wednesday, April 28: 9.15 a.m., "Affections of the Large Bowel", Dr. V. M. Coppleson and Dr. Bruce Hall; 10.45 a.m., "Operative Complications of Appendicitis: Immediate and Remote", Dr. B. T. Edey; 11.45 a.m., "The Stomach and Duodenum", Dr. J. E. Sherwood and Dr. V. J. Kinsella; 2.15 p.m., "The Pancreas and its Diseases", Dr. K. B. Noad and Dr. K. Starr; 3.45 p.m., "Diseases of the Liver and Biliary Tract", Dr. S. H. Lovell and Dr. A. W. Morrow.

Thursday, April 29: 9.15 a.m., seminar on cardio-vascular diseases, "Cardiac Arrhythmias", Dr. J. Sevier; 9.45 a.m., "Congestive Failure", Dr. J. Isbister; 10.45 a.m., "Congenital Heart Disease", Dr. J. K. Maddox; 11.15 a.m., "Coronary Disease", Dr. J. Markell; 11.45 a.m., panel discussion on cardiac problems in general practice; 2 p.m., at Sydney Hospital, demonstration of traumatic surgery, fractures and splints, Dr. P. Greenwell and Dr. A. I. Rhydderch; 3.45 p.m., "Some Aspects of Clinical Pathology in General Practice", the staff of the Kanematsu Institute of Pathology, Sydney Hospital.

Friday, April 30: 9.15 a.m., seminar on new drugs and therapeutic measures, Dr. A. J. Collins (chairman), Dr. A. W. Morrow, Dr. R. Jeremy, Dr. S. Nelson, Dr. K. S. Harrison, and Dr. W. J. Burke (to be confirmed).

Saturday, May 1: 9.30 a.m., demonstration by Dr. Guy Lawrance and staff at Broughton Hall Psychiatric Clinic.

Monday, May 3: 9.15 a.m., seminar on general medicine, "Ear, Nose and Throat in General Practice", Dr. G. Halliday; 10.45 a.m., "The Risks of Transfusion and Intravenous Injections", Dr. R. J. Walsh and Dr. C. R. Bickerton Blackburn; 2 p.m., demonstration of medical cases, at Royal Alexandra Hospital for Children, Professor L. Dods; 3.30 p.m., demonstration of surgical cases, Dr. T. Y. Nelson; 8 p.m., conference on medical education, Part I, "Training for General Practice", at the School of Public Health and Tropical Medicine.

Tuesday, May 4: 9.15 a.m., electrocardiographic conference, Dr. R. Blacket; 10.45 a.m., X-ray conference, Dr. A. R. Colwell, Dr. J. K. Maddox, Dr. N. Wyndham; afternoon, at the Northcott Neurological Centre, "Early Diagnosis of Cerebral Tumour", Dr. Eric Susman; demonstration of interesting neurological cases with X-ray films and electroencephalograms; Modern Concepts in the Treatment of Epilepsy, Dr. George Selby.

Wednesday, May 5: 9.15 a.m., seminar on gynaecological problems in general practice, Dr. George Stening (chairman); "Vaginal Discharge", Dr. M. Britnell Fraser; 9.45 a.m., "Anomalous Uterine Bleeding", Dr. Angus Murray; 10.45 a.m., "Problems of the Menopause", Dr. F. N. Chenhall; 11.15 a.m., "Management of Prolapse", Dr. H. K. Porter; 11.45 a.m., panel discussion on gynaecological problems in general practice; 2.15 p.m., seminar on obstetrical problems in general practice, Professor F. J. Browne (chairman); "Prevention of Severe Pre-Eclampsic Toxaemia and Eclampsia", Dr. R. B. C. Stevenson; 2.30 p.m., "Induction of Labour", Dr. K. S. Richardson; 2.45 p.m., "Surgical Complications during Pregnancy", Dr. A. A. Moon; 3 p.m., "Delayed Labour", Dr. R. C. Gill; 3.45 p.m., "quiz" session; 8 p.m., Seventh Annual Post-Graduate Oration, "The Life and Times of William Bland", Dr. A. M. McIntosh.

Thursday, May 6: 9.15 a.m., seminar on special subjects in general practice: "Dermatological Problems in General Practice", Dr. E. J. C. Molesworth; 10.45 a.m., "Management of Urinary Tract Infections", Dr. H. H. Pearson; 11.45 a.m., "Ophthalmology in General Practice", Dr. K. Armstrong; 2.15 p.m., surgical seminar, "Infections of the Hand", Dr. Noel Newton; "Varicose Veins and Ulcers", Dr. J. Loewenthal; film on "Self-Examination of the Breast".

Friday, May 7: 9.15 a.m., "Infectious Diseases", Dr. N. J. Symington; 10.45 a.m., "Recent Advances in Radiotherapy and the Use of Isotopes in Modern Medicine", Dr. H. J. Ham; 11.45 p.m., panel discussion on anaesthesia in general practice, Dr. H. Daly (chairman), Dr. A. D. Morgan, Dr. L. T. Shea, Dr. F. Leventhal; 2.15 p.m., question time, Dr. V. M. Coppleson (chairman), Dr. Selwyn Nelson, Dr. Bruce Williams, Dr. A. E. McGuinness, Dr. R. I. Furber.

All lectures will be held in the Stawell Hall, 145 Macquarie Street, Sydney, unless otherwise indicated.

Fee for attendance will be £12 12s. full time, or £6 6s. for one week or part time. Early written application is essential and should be made to the Course Secretary, The Post-Graduate Committee in Medicine, 131 Macquarie Street, Sydney. Telephones: BU 5238, BW 7483. Telegraphic address: "Postgrad Sydney."

Fees, fares and expenses for this course are allowable deductions for taxation under "Taxation—File No. AF/1865".

Week-End Course at Tamworth.

The Post-Graduate Committee in Medicine in the University of Sydney announces that, in conjunction with the Northern District Medical Association, a week-end course will be held at the Tamworth Base Hospital, Tamworth, on Saturday and Sunday, June 26 and 27, 1954. The programme is as follows:

Saturday, June 26: 2 p.m., registration; 2.30 p.m., symposium, "Rectal Bleeding in Children: Causes and Treatment"—(a) "Medical Diseases in Infancy", Dr. Kathleen Winning; (b) "Medical Diseases in Children", Dr. W. P. MacCallum; (c) "Surgical Causes", Dr. J. Steigrad, followed by discussion; 4.15 p.m., "Failure to Thrive during the First Year of Life", Dr. Kathleen Winning; 5 p.m., "Recognition and Treatment of Meningitis", Dr. W. P. MacCallum.

Sunday, June 27: 9.30 a.m., "quiz" session (subjects will include neonatal jaundice, treatment of talipes, torticollis, flat feet, indications for use of cortisone in children, management of the bronchitic child and demand feeding); 11.15 a.m., "The Infant as a Surgical Patient", Dr. J. Steigrad; 12 noon, subjects by local practitioners; 2 p.m., "Indications for Fluid Replacement in the Dehydrated Child with Particular Reference to Enteritis", Dr. Kathleen Winning; 2.45 p.m., "Poliomyelitis", Dr. W. P. MacCallum; 3.30 p.m., "Diagnosis and Management of Acute Intestinal Obstruction in Infants and Children", Dr. J. Steigrad.

The fee for attendance at the course will be £3 3s. Those wishing to attend are requested to notify Dr. G. Archbold, "Baranbali", Bridge and Denne Streets, West Tamworth, 4N, as soon as possible. Telephone: Tamworth B 351.

Research.

THE ROYAL SOCIETY.

Alan Johnston, Lawrence and Moseley Research Fellowship.

Applications are invited by the Council of the Royal Society for the Alan Johnston, Lawrence and Moseley Research Fellowship into the problems of human and animal

health and diseases and the biological field related thereto. The fellowship will be tenable at any place approved by the Council of the Royal Society. Candidates should supply the usual personal details and give the names of two referees. Testimonials will not be considered. Applicants and referees at a distance may write direct to the address given below, without first obtaining forms. The subject of the proposed research and the place at which it would be carried out, together with the name of the head of the department, should be given.

The appointment will be for two years in the first instance, from October 1, 1954, and will be renewable up to a maximum of five years. It will be subject to the conditions governing Royal Society research appointments. The stipend will be £1000 per annum, with annual increments of £75 per annum, with superannuation benefits to which the successful candidate will be required to contribute 5% of annual stipend and to which the Society will make a contribution of 10%.

Applications should be made on forms to be obtained from the Assistant Secretary, The Royal Society, Burlington House, London, W.1, and should be received as early as possible, in any case not later than April 30, 1954.

Stothert Research Fellowships.

Applications are invited by the Council of the Royal Society for two Stothert Research Fellowships in the field of medicine, including the sciences on which medical knowledge is based. Each fellowship will be tenable in any hospital, medical school or other appropriate research institution or university department in the British Isles or at any other place approved by the Council of the Royal Society. Candidates, who must be of British nationality, should supply the usual personal details and give the names of two referees. Testimonials will not be considered. Applicants and referees at a distance may write direct to the address given below, without first obtaining forms. The subject of the proposed research, and the place at which it would be carried out, together with the name of the head of the department, should be given.

The appointments will be for two years in the first instance, from October 1, 1954, and may be renewed annually up to a total of four years. The stipend will be £600 per annum, with increments of £50 per annum, and superannuation benefits to which the successful candidate will be

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED FEBRUARY 6, 1954.¹

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.	Australian Capital Territory.	Australia.
Acute Rheumatism	1	4(3)	3(3)	8
Amoebiasis
Ancylostomiasis
Anthrax
Bilharziasis
Brucellosis	1(1)	1
Cholera
Chorea (St. Vitus)
Dengue
Diarrhoea (Infantile)	7(5)	4(2)	5(5)	..	3(1)	22
Diphtheria	5(4)	6(3)	..	1	..	7
Dysentery (Bacillary)	1(1)	1(1)	9(6)	10
Encephalitis	2(1)	2
Filaria
Homologous Serum Jaundice
Hydatid
Infective Hepatitis	15(4)	4	19
Lead Poisoning
Leprosy
Lepthospirosis
Malaria
Meningococcal Infection	1(1)	4(3)	..	1(1)	3	1(1)	10
Ophthalmia	3	3
Ornithosis
Paratyphoid
Plague
Poliomyelitis	10(4)	7(6)	1	6(5)	8(6)	1	33
Puerperal Fever	1(1)	1
Rubella	11(5)	7(4)	15
Salmonella Infection	1(1)	1
Scarlet Fever	4	11(7)	5(3)	1	..	1(1)	22
Smallpox
Tetanus	1	1
Trachoma	1	1
Trichinosis
Tuberculosis	28(17)	19(10)	1	7(1)	6(4)	3	64
Typhoid Fever
Typhus (Flea-, Mite- and Tick-borne)	1(1)	1(1)	2
Typhus (Louse-borne)
Yellow Fever

¹ Figures in parentheses are those for the metropolitan area.

required to contribute 5% of annual stipend and to which the Society will make a contribution of 10%.

Applications should be made on forms to be obtained from the Assistant Secretary, The Royal Society, Burlington House, London, W.1, and should be received as early as possible and not later than April 30, 1954.

Notice.

NATIONAL ASSOCIATION FOR THE PREVENTION OF TUBERCULOSIS IN AUSTRALIA (NEW SOUTH WALES DIVISION).

Laennec Society.

A CLINICAL MEETING of the Laennec Society will be held at the Anti-Tuberculosis Association Chest Clinic, at Crown Street, Sydney, on Monday, March 22, 1954, at 8 p.m. Members are invited to bring any guests who may be interested.

SECTION OF PREVENTIVE MEDICINE, VICTORIAN BRANCH OF THE BRITISH MEDICAL ASSOCIATION.

THE first meeting for 1954 of the Section of Preventive Medicine of the Victorian Branch of the British Medical Association will be held in the Medical Society Hall, 426 Albert Street, East Melbourne, at 4.30 p.m. on Thursday, March 11. Dr. N. H. Andrews, Deputy Director of Child Health (Dental), Department of Health, will give an address entitled "Fluoridation of Water and its Place in the Prevention of Dental Caries". The discussion will be opened by Dr. E. J. Crowe. All members of the Branch are invited to be present.

Medical Practice.

NATIONAL HEALTH (PENSIONERS' MEDICAL SERVICES COMMITTEE OF INQUIRY) REGULATIONS.

THE following notice appeared in the *Commonwealth of Australia Gazette*, Number 83, of December 23, 1953.

REPRIMAND OF MEDICAL PRACTITIONER.

I, Earle Page, the Minister of State for Health, hereby give notice, in pursuance of sub-regulation (3.) of Regulation 26 of the National Health (Pensioners' Medical Services Committees of Inquiry) Regulations that I have this day reprimanded Oscar Rychter, of 761 Darling Street, Rozelle, in the State of New South Wales, medical practitioner, following receipt of a report and recommendation concerning his conduct in relation to the provision of medical services to pensioners and their dependants under an arrangement made by the Director-General of Health under section 7 of the *National Health Service Act 1948-49* and the *National Health (Medical Services to Pensioners) Regulations*.

Dated this eleventh day of December, 1953.

EARLE PAGE,
Minister of State for Health.

Deaths.

THE following deaths have been announced:

STEPHEN.—Edgar Horatio Milner Stephen, on February 10, 1954, at Sydney.

MATTHEWS.—Walter Frederick Matthews, on February 14, 1954, at Orange, New South Wales.

NIALL.—John Henry Niall, on February 15, 1954, at Toorak, Victoria.

WATSON.—Arthur Harrison Edward Watson, on February 12, 1954, at Adelaide.

FOY.—Donovan Sylvester Foy, on February 19, 1954, at Sydney.

LEARY.—Thomas Garnet Stirling Leary, on February 20, 1954, at Sandringham, Victoria.

Nominations and Elections.

THE undermentioned has applied for election as a member of the New South Wales Branch of the British Medical Association:

Hoyle, Mary Beatrice, M.B., B.S., 1953 (Univ. Adelaide), Queanbeyan District Hospital, Queanbeyan, New South Wales.

Diary for the Month.

MARCH 9.—New South Wales Branch, B.M.A.: Executive and Finance Committee.

MARCH 12.—Queensland Branch, B.M.A.: Council Meeting.

MARCH 15.—Victorian Branch, B.M.A.: Finance Subcommittee.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney): All contract practice appointments in New South Wales.

Victorian Branch (Honorary Secretary, Medical Society Hall, East Melbourne): Associated Medical Services Limited; all Institutes or Medical Dispensaries; Australian Frudential Association, Proprietary, Limited; Federal Mutual Medical Benefit Society; Mutual National Provident Club; National Provident Association; Hospital or other appointments outside Victoria.

Queensland Branch (Honorary Secretary, B.M.A. House, 225 Wickham Terrace, Brisbane, 317): Brisbane Associated Friendly Societies' Medical Institute; Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 178 North Terrace, Adelaide): All Contract Practice appointments in South Australia.

Western Australian Branch (Honorary Secretary, 205 Saint George's Terrace, Perth): Norseman Hospital; all Contract Practice appointments in Western Australia. All government appointments with the exception of those of the Department of Public Health.

Tasmania: Part-time specialist appointments for the north-west coast of Tasmania.

Editorial Notices.

MANUSCRIPTS forwarded to the office of this journal cannot under any circumstances be returned. Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary be stated.

All communications should be addressed to the Editor, THE MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer Street, Glebe, New South Wales. (Telephones: MW 2651-2.)

Members and subscribers are requested to notify the Manager, THE MEDICAL JOURNAL OF AUSTRALIA, Seamer Street, Glebe, New South Wales, without delay, of any irregularity in the delivery of this journal. The management cannot accept any responsibility or recognize any claim arising out of non-receipt of journals unless such notification is received within one month.

SUBSCRIPTION RATES.—Medical students and others not receiving THE MEDICAL JOURNAL OF AUSTRALIA in virtue of membership of the Branches of the British Medical Association in the Commonwealth can become subscribers to the journal by applying to the Manager or through the usual agents and booksellers. Subscriptions can commence at the beginning of any quarter and are renewable on December 31. The rate is £5 per annum within Australia and the British Commonwealth of Nations, and £6 10s. per annum within America and foreign countries, payable in advance.